

November 2014

## NIEHS Spotlight



### [NCATS director inspires innovation in translation](#)

In his talk Oct. 2, Christopher Austin, M.D., National Center for Advancing Translational Sciences director, shared innovations that are putting science to good use.



### [NIEHS contributes to big NIH investment in biomedical research data](#)

As part of a broad NIH grant program announced Oct. 10, NIEHS is helping make use of new biomedical data sets.



### [Environmental health literacy meeting explores research for better communication](#)

More than one hundred people joined in the Oct. 22-24 NIEHS Partnerships for Environmental Public Health meeting — in person and via watch parties.



### [Economist puts dollar figures on impact of underserved and minority training](#)

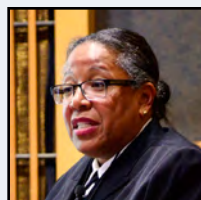
The NIEHS Worker Training Program hosted a talk Oct. 6 by College of the Holy Cross labor economist Brian Engelhardt, Ph.D.



### [Workshop explores ways to protect workers from climate change](#)

The NIEHS Worker Training Program workshop Oct. 7-8 focused on the health risks workers face as climate change becomes more prominent.

## Clinical Feature



### [NIA study focuses on health disparities](#)

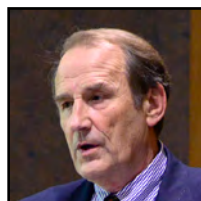
The NIEHS Office of Human Research Compliance continued its seminar series Oct. 15 with a discussion of recruiting and retaining participants for a clinical research study.

## Science Notebook



### [Distinguished lecture explores contradictory role of Hedgehog signaling](#)

Beachy shared discoveries on the role of Hedgehog signaling in molecular pathways and its promise for inhibiting cancer.



### [Distinguished lecture examines the rise of allergic disease](#)

Researchers aren't sure what is behind the emergence of allergic diseases, but allergist Thomas Platts-Mills, M.D., Ph.D., has several theories about their origins.



### [The 13th Report on Carcinogens includes four newly reviewed substances](#)

In the Oct. 2 release of the 13th RoC, ortho-toluidene was listed as known to be a human carcinogen, and three others are added as reasonably anticipated to cause cancer.

## NIEHS Spotlight



### [High-profile NIH funding awards go to NIEHS grantees](#)

Four NIEHS grantees are among the 85 winners of 2014 High Risk-High Reward program awards announced Oct. 6 by NIH Director Francis Collins, M.D., Ph.D.



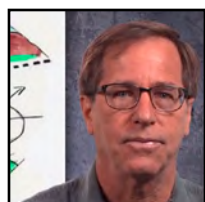
### [NIEHS joins WHO Chemical Risk Assessment Network meeting](#)

With support from NIEHS, the organization held its first meeting Oct. 8-10 in Paris, to explore and address the public health risks posed by toxic chemicals.



### [Research!America honors Olden for advocacy](#) 🏆

Next spring, NIEHS and NTP Director Emeritus Kenneth Olden, Ph.D., will be one of five people honored with a 2015 Research!America Advocacy Award.



### [Bioregional planning to improve public and environmental health](#)

Researchers funded in part by NIEHS propose a One Border/One Health approach to improve public health in the U.S.-Mexico borderlands.



### [Annual FASEB BioArt awards include NIEHS grantee](#) 🏆 Video

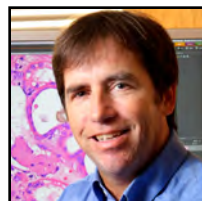
An image by an NIEHS grantee and colleagues is a winner in the Federation of American Societies for Experimental Biology BioArt competition.



### [NIEHS fellow begins career in biopharma](#)

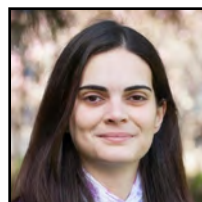
Raj Gosavi, Ph.D., NIEHS postdoc and Environmental Factor contributor, lands a local position in pharmaceutical research.

## Science Notebook



### [Veterinary pathology group chooses Malarkey as 2015 president-elect](#)

NTP Pathologist David Malarkey, D.V.M., Ph.D., was elected this summer as 2015 president-elect of the American College of Veterinary Pathologists.



### [Ethnic ancestry among Latinos influences asthma risk](#)

NIEHS-funded researchers demonstrate that among U.S. Latino children, the risks of developing asthma vary with genetic ancestry.



### [NIEHS scientists participate in 2014 NIH Research Festival](#)

Despite continuing limitations on travel, several NIEHS scientists and trainees presented at the 2014 NIH Research Festival Sept. 22-24 in Bethesda, Maryland.



### [NCSOT fall meeting highlights "Hot Topics in Toxicology"](#)

The North Carolina chapter of the Society of Toxicology held its annual fall meeting Oct. 9 in the Rodbell Auditorium at NIEHS.



### [Summit attendees translate big data into useful knowledge](#)

Some 30 NIEHS scientists joined more than 200 representatives from industry, academia, regulatory agencies, and nongovernmental organizations Sept. 29-30 for the workshop.



### [Nanotechnology work leads to award for NIEHS grantee](#) 🏆 Video

Somenath Mitra, Ph.D., received the New Jersey Institute of Technology Excellence in Research award Oct. 2 for his work on carbon nanotubes.

## NIEHS Spotlight



### [Taking science to a wider audience at NIEHS](#)

An Oct. 1 event launched a new series for NIEHS nonscientific staff, with scientists sharing their research in easy-to-understand talks.

## Inside the Institute



### [NIEHS celebrates 2014 Fall Fest](#)

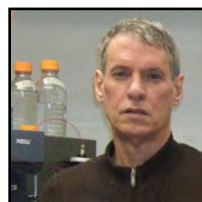
Scientists and employees from across the institute flocked to the main building Oct. 23 for the 2014 Fall Fest as part of the 2014 Combined Federal Campaign drive.

## Science Notebook



### [This month in EHP](#)

November's Environmental Health Perspectives addresses environmental aspects of stunted growth and the major sources of water pollution, nitrogen and phosphorous.



### [Upcoming Falk Lecture to feature Frank Gonzalez](#)

Frank Gonzalez, Ph.D., of the National Cancer Institute, will present the Falk Lecture Nov. 18, highlighting his research on cytochrome P450 and xenobiotic receptors.

## Extramural Research

### [Extramural papers of the month](#)

- [BPA linked with endometriosis](#)
- [Uranium exposure linked with lupus](#)
- [Predicting placement of epigenetic modifications](#)
- [Environment stronger than genetics for eosinophilic](#)

## Intramural Research

### [Intramural papers of the month](#)

- [NTP helps develop technique for detecting chemicals that disrupt testis function](#)
- [Pesticide use may increase depression risk among farmers](#)
- [DNA replication errors in yeast offer new insight into cancer research](#)
- [Genistein exposure alters the action of glucocorticoids](#)
- [Orphan receptor regulates lipid metabolism](#)

## Calendar of Upcoming Events

- **Nov. 3-4**, in Rodbell Auditorium, 8:00 a.m.-5:00 p.m. — NIEHS and National Institute of Neurological Disorders and Stroke conference — “Parkinson’s Disease: Understanding the Environment and Gene Connection” [webcast](#)
- **Nov. 4-5 (offsite event)**, at the North Carolina Biotechnology Center — Environmental Health Collaborative “Exposure Science in the 21st Century: Role of Citizens and Communities”
- **Nov. 6-7**, in Rodbell Auditorium and Building 101 mall — NIEHS Science Days awards and poster competition
- **Nov. 10**, in Rodbell Auditorium, 2:30-3:30 p.m. — First NIEHS Veterans Day Celebration
- **Nov. 10-11 (offsite event)**, at the Keck Center in Washington, D.C. — Institute of Medicine Roundtable on Environmental Health Research, Science, and Medicine, “Environmental Impacts on Obesity” (contact [Kathleen Stratton](#), NAS)
- **Nov. 12 (offsite event)**, at the National Institutes of Health Lister Hill Auditorium in Bethesda, Maryland, 8:30 a.m.-5:00 p.m. — 3rd American Society for Cellular and Computational Toxicology Annual Meeting, “Where Chemistry and Biology Meet: AOPs [Adverse Outcomes Pathways] as a Framework for Advancing Toxicology”
- **Nov. 12-14 (offsite event)**, at the Dolce Hayes Mansion and Conference Center in San Jose, California — Superfund Research Program annual meeting, [register](#)
- **Nov. 18**, in Rodbell Auditorium, 11:00 a.m.-noon — Hans L. Falk Memorial Lecture, “Search for Cancer Biomarkers Using Metabolomics,” by [Frank Gonzalez, Ph.D.](#)
- **Nov. 18**, in the Executive Conference Room, 2:00-3:00 p.m. — Big Picture Small Talk, with Richard Kwok, Ph.D., and Scott Auerbach, Ph.D., discussing “Environmental Accidents”
- View More Events: [NIEHS Public Calendar](#)



## NCATS director inspires innovation in translation


By Shannon Whirlledge

During an Oct. 2 seminar, “Catalyzing Translational Innovation,” National Center for Advancing Translational Sciences (NCATS) Director Christopher Austin, M.D., explained that the establishment of the new center enables the National Institutes of Health (NIH) to move in exciting new directions.

While [Austin](#) is relatively new to his position at [NCATS](#), NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., who hosted Austin’s talk, stressed Austin’s long and rich interaction with NIEHS and NTP, through his work with the Tox21 chemical toxicity screening project. Austin described the [Tox21](#) project as the single best collaboration he has had in his career.





*“Everything at NCATS is an experiment. We are constantly evolving,” said Austin. (Photo courtesy of Steve McCaw)*



**Linked video:**  
[Watch this NCATS video explaining the work NCATS is doing to find solutions to health challenges. \(5:15\)](#)

Christopher P. Austin, M.D.  
Director, National Center for Advancing Translational Sciences

(Launches in new window)

Download Media Player:  Flash 

### Discovering how to fix what is broken

According to Austin, though we now know more about ourselves and how our bodies work than ever before, the global public health community is not keeping up with these advances. “Understanding why something is broken and understanding how to fix it are fundamentally different,” he explained. For instance, because toxicity accounts for 30 percent of drug failure, predictive toxicology is at the top of the to-do list at NCATS.



*In her introduction, Birnbaum revealed that, in addition to his rich history in science and medicine, Austin is an opera singer. (Photo courtesy of Steve McCaw)*

The Tox21 collaborative effort by NTP, NCATS, the U.S. Environmental Protection Agency, and the U.S. Food and Drug Administration is making huge strides toward improving predictive toxicity assessment methods. Austin described it as the no compound left behind act, because scientists are testing more than 10,000 chemical compounds with a high-throughput robotic screening system.

## Innovation through crowdsourcing

This large-scale system has generated roughly 50 million data points, and at a center where everything is a collaboration, this volume of data provides an opportunity for yet another type of collaboration. NCATS is crowdsourcing data analysis to develop computational models that can better predict toxicity. This type of data transparency represents one step toward overcoming obstacles to translational research.

“If we want to comprehensively understand and predict toxicity, then we must know all the biological pathways in the human body,” said Austin, pointing out that it would be a significant challenge for individual scientists. In an effort to overcome the individualistic nature of research, the Tox21 researchers are designing an integrated pathway database, known as BioPlanet, to facilitate development and prioritization.



*Shepherd Schurman, M.D., acting medical director of the NIEHS Clinical Research Unit, and Serena Dudek, Ph.D., head of the NIEHS Synaptic and Developmental Plasticity Group, were among the full house for Austin's talk. (Photo courtesy of Steve McCaw)*

## Tissue on a chip

In addition to predicting toxicity, the ability to predict effectiveness would drastically reduce time spent on candidate drugs that ultimately fail in human clinical trials. Meeting this challenge requires a unique pairing of biology and engineering.

Led by NCATS, NIH is supporting researchers across the country to develop [tissues on a chip](#) that can screen compounds for toxicity, effectiveness, and safety. These chips can mimic the complex functions of the human body, including major body organs, on individual chips, and may revolutionize preclinical testing of potential treatments.



*Austin spoke highly of Raymond Tice, Ph.D., in blue checked shirt, who will be retiring next year. “He is one of the best collaborators ever,” Austin said. (Photo courtesy of Steve McCaw)*

## Letting biology define the answer

Each year, around 15,000 people in the U.S. are diagnosed with chronic lymphocytic leukemia, the most common form of leukemia in adults. Unfortunately, it is generally considered incurable and prognosis varies. What these patients do have is an abundance of cells, and that is just what was needed to search for new drugs that selectively kill leukemia cells. Through a collaboration with the National Heart, Lung, and Blood Institute, NCATS was able to get patient samples onto the screening platform within one day, looking for drugs that will kill the leukemia cells, but not harm normal donor immune cells.

Unexpectedly, the arthritis drug auranofin was identified as just such a selective cytotoxic drug, demonstrating the ability of the NCATS process to discover that a drug approved for one use may be effective for an apparently unrelated condition. Within a year of this discovery, the collaborative team was able to complete all preclinical trials necessary to support clinical trials in patients, not to mention shedding new light on the basic biology of the disease.



## A rapid-response innovation driver

NCATS is the most recently formed research center at the National Institutes of Health (NIH). At the helm, Austin hopes this center will become what he called a rate of change institute.

He defined translation as the process of turning observations in the lab and clinic into interventions that improve health of individuals and the public. “NCATS lets biology define what the answer is, rather than what preconceived notions say the answer should be,” said Austin.

(Shannon Whirlledge, Ph.D., is a research fellow in the NIEHS Molecular Endocrinology Group.)

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## NIEHS contributes to big NIH investment in biomedical research data

*By Joe Balintfy*

As part of wide-ranging grants announced Oct. 10 by NIH, NIEHS is helping develop new strategies to analyze and make good use of the explosion in complex biomedical data sets, often referred to as Big Data. NIEHS involvement in the NIH Big Data to Knowledge (BD2K) investment spans all areas of emphasis, including training, research centers, and data discovery.

“NIEHS has had a role in developing BD2K initiatives through our participation on numerous workgroups over the past 18 months,” said Allen Dearry, Ph.D., director of the NIEHS Office of Scientific Information Management and NIEHS representative to the BD2K Executive Committee.

### Big data centers

“We are managing the career development portion of this nearly \$32 million investment,” said Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training. “We are also participating in the grants establishing Centers of Excellence for Big Data Computing.”

The 11 [centers](#) will develop innovative approaches, methods, software, tools, and other resources to enhance access to data and the ability to make new discoveries using it, according to an NIH [press release](#). Development efforts will focus on specific research questions, yet the centers’ output is expected to be more generally relevant to aspects of big data science, such as data integration and use, analysis of genomic data, and managing data from electronic health records.



*“We have been instrumental in ensuring inclusion of environmental and exposure data within the diverse types of big data addressed by BD2K,” said Dearry. (Photo courtesy of Steve McCaw)*

## Data science training and workforce development

The Training and Career Development in Biomedical Big Data [awards](#) support education and training of researchers who will specialize in data science fields, as well as those whose work may require expertise in the use or generation of large amounts of data and data resources.

“Some training projects include brain imaging studies, identifying healthy behaviors that may reduce risk of heart disease and diabetes, and harnessing the largely untapped potential of social media data to capture social and cultural processes with potential health impact,” said NIEHS Program Director Carol Shreffler, Ph.D.

Teams at large research universities and academic medical centers may have bioinformatics and data support, but individual scientists in the biomedical research community may not, and many have not been trained to access and analyze large data sets.



*“The training programs span a wide range of big data research areas,” said Shreffler. (Photo courtesy of Steve McCaw)*

# BIOMEDICAL BIG DATA EXPLOSION

## NIH National Center for Biotechnology Information DATA STORAGE

In **1990** fit on  
3 floppy disks



In **1993** fit on  
1 CD-ROM



In **2014** could fill  
**400 MILLION**  
4-drawer filing cabinets



## Types of BD2K Awards



Enabling Data  
Utilization



Analysis Methods  
and Software



Enhancing  
Training



Centers of  
Excellence



Big Data to Knowledge (BD2K) is an initiative of the National Institutes of Health

*Big data comes along with challenges such as locating data, lack of data standards, and lack of tools to access and analyze data sets.*



## Data discovery

NIH also launched an effort to pilot a [Data Discovery Index](#) (DDI), which will catalyze the discoverability, accessibility, and citation standards for biomedical big data. “Currently, there is no easy query or search infrastructure that can help identify the presence and availability of relevant data sets,” said Becky Boyles, a member of the NIH team overseeing this project and an NIEHS data scientist.

Boyles explained that data are found in an increasing number and variety of different repositories or web sites, when they are available at all. “The intent of establishing a DDI is to help researchers find, reuse, and cite relevant publicly available datasets related to their scientific question of interest,” she said.

## Big data is a big deal

Studies generating billions of data points continue to proliferate. For example, environmental studies gather data on multiple exposures and health outcomes, epidemiological studies examine thousands of participants for health and disease patterns, large disease-oriented efforts seek the genomic underpinnings of illnesses, and other projects look to identify all functional elements in the human genome.

“Mammoth data sets are emerging at an accelerated pace in today’s biomedical research,” said NIH Director Francis S. Collins, M.D., Ph.D. “The potential of these data, when used effectively, is quite astounding.”

(Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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# Environmental health literacy meeting explores research for better communication

*By Joe Balintfy*

More than 120 researchers, community partners, and health care professionals, as well as federal, state, and tribal representatives, came together at NIEHS Sept. 22-24 to advance the field of environmental health literacy. Dozens more joined remotely via [watch parties](#) in California, Georgia, Kentucky, Michigan, Minnesota, Montana, Oregon, and Washington.

Environmental health literacy has recently emerged as a distinct field within health education and risk communication. The theme of the annual [meeting](#) of the NIEHS Partnerships for Environmental Public Health (PEPH), Communication Research in Environmental Health Sciences — Environmental Health Literacy, emphasized the importance of conducting research to better understand how to effectively communicate with communities.



*Birnbaum set the stage for the meeting by emphasizing the importance of community outreach and engagement that can contribute to environmental health literacy. (Photo courtesy of Steve McCaw)*

“We cannot promote healthier lives without people getting involved, and we cannot do that without excellent communication,” said NIEHS and National Toxicology Program Director Linda Birnbaum, Ph.D., in her opening remarks. “We need to shift our focus from solely the production of educational and risk communication messages, and apply the principles of communication research to discover the elements that will best support environmental health literacy.”

### Communication is key

The meeting planners arranged for presentations on different aspects of communication research, as well as a number of interactive discussions among the diverse range of attendees about how to be successful with environmental public health messages.

“What I observed from the meeting was a lot of active conversation from the different partners, whether community resident, researcher, health care professional, or federal representative,” said Liam O’Fallon, program lead for [PEPH](#). In a series of small table discussions, attendees shared different communications approaches and the challenges of how to apply communications research methodologies to environmental public health efforts.

O’Fallon and Symma Finn, Ph.D., health scientist administrator in the NIEHS Division of Extramural Research and Training, presented on two key aspects of communication research — how to quantify and measure stages of environmental health literacy, and the role that cultural influences play in public understanding of environmental risk.

Finn suggested that the numerous cultural influences, such as media and films, that underlie public understanding of environmental risk need to be taken into account when developing health risk messages. She noted other presentations at the meeting explored best practices for targeting messages to specific audiences.

“There were many excellent talks that provided examples of current research efforts, such as the work to develop Indian health indicators for use in tribal communities, the use of geographic information systems to communicate risk in an easily understood visual format, and successful efforts to target and educate health professionals about environmental health risks,” said Finn.

## What is environmental health literacy?

Early in the meeting, O’Fallon shared a definition of environmental health literacy, to spark discussion within the context of the NIEHS commitment to communication and community engagement. “At its most basic level, environmental health literacy is the understanding of the link between environmental exposures and health,” he said.

O’Fallon emphasized the underlying issue of connecting the public perception of human health to how health can be affected by environmental exposures. He also proposed an environmental health literacy model, adapted from [Bloom’s Taxonomy of Educational Objectives](#), which could be used to measure levels of environmental health literacy and to examine impacts of communication interventions.

Referring to closing comments by Gwen Collman, Ph.D., director of the NIEHS Division of Extramural Research and Training, O’Fallon said, “She took that model and populated it with the types of research questions you might ask to achieve comprehension at each of its literacy levels.”



*From left, McIntosh-Kastrinsky and Silk shared the importance of listening as part of the communication and collaboration process. (Photo courtesy of Joe Balintfy)*

## Group discussions and collaboration

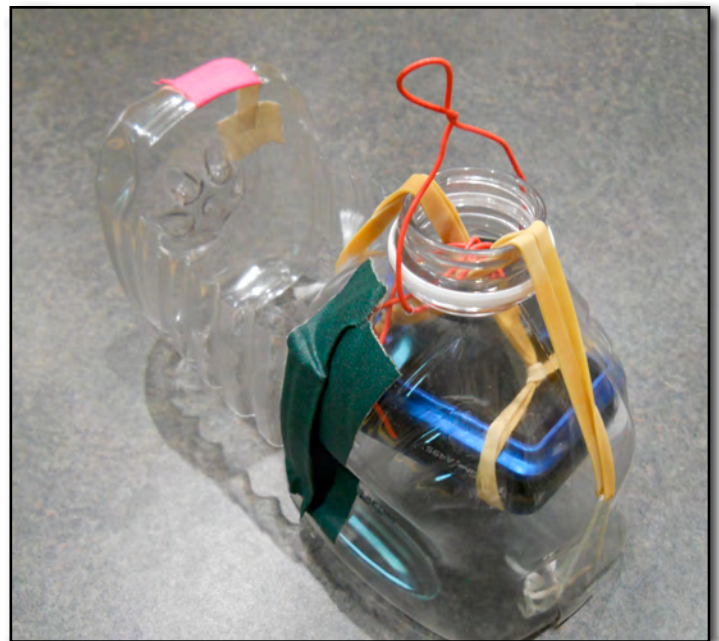
The three-day meeting fostered collaboration by providing for group discussions after presentations, a series of workshops, and breaks for attendees to view posters and to network.

“I think there were a lot of opportunities for communication researchers to meet environmental scientists,” pointed out Kami Silk, Ph.D., associate dean of graduate studies and professor of communication at Michigan State University. She shared a table with Rachel McIntosh-Kastrinsky, an environmental health fellow at the U.S. Environmental Protection Agency, who echoed the feeling that there is room for even more collaborative work between environmental health science researchers and communication researchers. “Scientists and communications people — we all need to come together,” she said.

Participants also emphasized that new media, including social media, are forces that can help push environmental health literacy and public health forward.



*Sara Wylie, Ph.D., assistant professor of anthropology at the Social Science and Environmental Health Research Institute at Northeastern University, gave one of 11 workshops. Wylie showed how balloon mapping can be a community-based approach to environmental health research (see related [story](#)). (Photo courtesy of Joe Balintfy)*



*Wylie's homemade satellite includes a reused plastic juice bottle, rubber band harness, and inexpensive digital camera, which can detect hydrogen sulfide contamination and map thermal pollution. (Photo courtesy of Joe Balintfy)*

(Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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# Economist puts dollar figures on impact of underserved and minority training

By Eddy Ball

The NIEHS Worker Training Program hosted a talk Oct. 6 by College of the Holy Cross labor economist Bryan Engelhardt, Ph.D., on the program assessment he is conducting with colleagues Robert Baumann, Ph.D., and Katherine Kiel, Ph.D.

Through a contract with NIEHS, the team is nearing completion of a comprehensive economic impact analysis of the Minority Worker Training Program. Since 1995, the initiative has prepared 9,600 participants across the U.S. for skilled jobs in construction, many of them directly related to environmental improvement and remediation.

Engelhardt's presentation was hosted by NIEHS industrial hygienist Sharon Beard, founding coordinator of the Minority Worker Training Program, who was honored by the American Public Health Association in 2013 for her service to the health and safety of minority workers (see [story](#)).

Through Engelhardt's research, Beard is now striving to quantify the economic benefits of the program to participants and society as a whole. This effort, Engelhardt explained at the beginning of his talk, is consistent with goal 10 of the NIEHS 2012-2017 [strategic plan](#), to measure the economic benefits and the comparative effectiveness of NIEHS initiatives, especially in public health and community engagement.

## Wages, safety, taxes, and crime

"There was a huge employment bump [for program participants]," Engelhardt told the audience. "Sixty percent were more likely to be placed in [higher paying, full-time] jobs."

For minority workers with low wages, unemployment or underemployment, and experience in the criminal justice system, the steady paycheck for working more hours and a nearly 33 percent boost in pay after completing training was transforming. Over an average lifetime, compared with people of similar backgrounds who did not participate in minority worker training, graduates and their families benefited significantly and made positive contributions to society.



"How conservative can I make this number?" Engelhardt asked, as he reached the end of his presentation and played devil's advocate with his estimates. (Photo courtesy of Steve McCaw)



"We're just ecstatic," Beard said of the prospect of solid metrics to evaluate the training program. (Photo courtesy of Steve McCaw)

The most favorable estimates of value added over a lifetime for the 9,600 participants and others include:

- Higher earnings over a lifetime — estimated at a total of \$1.6 billion
- Savings from improved safety on the job — \$181.2 million in reduced workplace injury costs
- Savings for employers — lower turnover resulting in a savings of \$23.7 million in reduced hiring and training costs
- Savings for taxpayers and victims of crime — an estimated reduction of \$22.1 million in crime-related costs
- Increased tax collections and reductions in government transfers, such as the earned income credit — an estimated \$711.6 million boost for governments

With one-third of participants transitioning to jobs in environmental remediation, Engelhardt said there were obviously environmental improvements that resulted from the training. However, he was reluctant to speculate on a dollar value, because of the difficulty in quantifying the effects on public health, property values, and community perception.

Equally difficult to measure are the long-range and intangible benefits of training and job security, such as the effects on children of participants, family stability, and self esteem.

A number of questions remain in this emerging field of health economics, before Engelhardt will have what he described as a bullet-proof methodology for measuring effectiveness. Still, no matter how critically he examined the metrics the team used to estimate the impact of minority worker training over nearly two decades, one thing was clear — without question, for participants, government, fellow citizens, and the environment, the program has paid for itself many times over.

(For more information about the Minority Working Training Program, including a guide to best practices, and other initiatives supported by the NIEHS Worker Training Program, visit the National Clearinghouse for Worker Safety and Health Training [website](#).)

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*Representing the Worker Training Program's contractor, MDB Inc., Larry Reed underscored the need for a detailed understanding of economics to frame impact assessment. (Photo courtesy of Steve McCaw)*



*The talk attracted NIEHS staff involved in grants management and program evaluation, such as Nicole Popovich, left, and Kristi Pettibone, Ph.D. (Photo courtesy of Steve McCaw)*



# Workshop explores ways to protect workers from climate change

By Tara Failey

The NIEHS Worker Training Program held a workshop Oct. 7–8 focused on the health risks workers face as consequences of climate change become more prominent. [Workshop](#) participants explored lessons learned and best practices to prepare workers for climate change effects. Participants also discussed curricula that can be developed to build a more resilient and sustainable workforce and community.

The workshop, held at NIEHS headquarters in Research Triangle Park, North Carolina, followed the semiannual Worker Training Program Awardee Meeting Oct. 6 in the same location. The awardees include a strong network of nonprofit organizations, universities, and unions, which provide occupational safety and health education to workers.

The framework for the workshop was the program’s draft Climate Change Vulnerability Assessment [Report](#), which reviews the available literature on worker health and climate change, and assesses available training and resources.

## Unique vulnerabilities of workers

“Workers are the climate canaries in the coal mine,” said Cora Roelofs, Sc.D., of Tufts University, during a panel discussion. “But occupational health and safety concerns have been largely ignored in climate change discussions.”

Speaking to this concept, NIEHS Senior Advisor for Public Health John Balbus, M.D., cited research showing that climate change will have a severe impact on human health and that workers are among those who will be most impacted. Underscoring key messages in the third [National Climate Assessment](#), Balbus discussed how workers may be exposed to conditions that the general public can more easily avoid, such as severe heat, increased UV radiation, and heavy rain.

## Possible paths forward

David Foster, of the Department of Energy Office of the Secretary, endorsed a multi-tiered approach to addressing problems facing workers. His approach includes recommending that each workplace conduct a climate risk assessment, and developing climate adaptation plans at the state and federal level that also consider employee training.



*Roelofs discussed new frameworks for considering climate change and occupational safety and health. (Photo courtesy of Steve McCaw)*



*Balbus shared findings of the Third National Climate Assessment, released earlier this year, emphasizing that climate change is already impacting both the health of workers and the general public. (Photo courtesy of Steve McCaw)*



Foster highlighted how any approach must involve a coordinated shift toward use of renewable energy technologies, such as those being improved and developed by the [National Renewable Energy Laboratory](#). “We have to improve technologies to reduce greenhouse gases, and in doing so, we will also reap economic and societal benefits,” Foster said.

His recommendations were complemented by discussions on how to maximize existing resources, and develop new resources. For instance, the [National Clearinghouse for Worker Safety and Health Training](#) has a series of curricula on climate change-related topics, such as flood response and hurricane preparedness, which could be more widely distributed and shared.

Further, WTP awardees could connect with organizations like the Climate Change Occupational Safety and Health [Work Group](#) of the National Institute of Occupational Safety and Health. Participants also raised the need for improved sharing of resources, and highlighted use of materials developed by other organizations, such as the American Chemical Society’s Climate Science [Toolkit](#).

Roelof issued a final challenge to the WTP awardee community. “[We] are the planning and response vanguard for climate change...and need to push for worker training in a more audacious way,” she said.

(Tara Failey is a communication specialist with MDB Inc., contractor for the NIEHS Division of Extramural Research and Training.)

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*Foster shared insights on how the U.S. Department of Energy and other employers can actively engage in assessing and protecting workers from the impacts of climate change. (Photo courtesy of Steve McCaw)*

## High-profile NIH funding awards go to NIEHS grantees

*By Eddy Ball*

Four NIEHS grantees are among the 85 winners of 2014 National Institutes of Health (NIH) High Risk-High Reward program awards announced Oct. 6 by NIH Director Francis Collins, M.D., Ph.D.

According to the NIH [press release](#), the funding awards will support scientists proposing highly innovative approaches to major contemporary challenges in biomedical research. The winners will share approximately \$141 million in grants funded by the NIH Common Fund and multiple NIH institutes, centers, and offices.

“Supporting innovative investigators with the potential to transform scientific fields is a critical element of our mission,” Collins wrote in the press release. “This program allows researchers to propose highly creative research projects across a broad range of biomedical and behavioral research areas that involve inherent risk, but have the potential to lead to dramatic breakthroughs.”

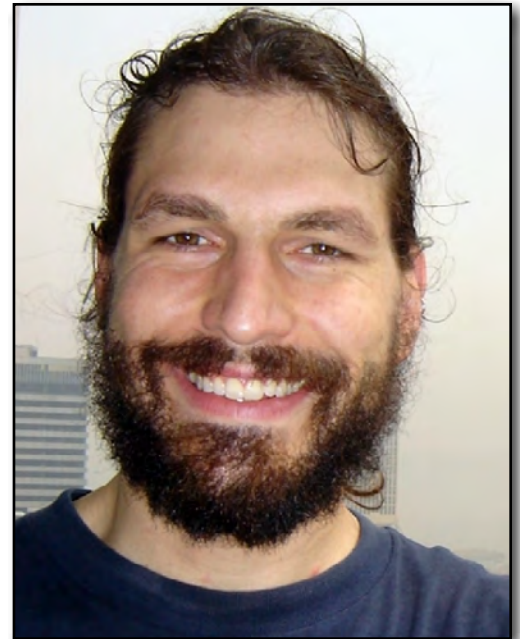
## The NIEHS winners

NIEHS grantees include [Donna Spiegelman, Sc.D.](#), of the Harvard School of Public Health, and [Oliver Rando, M.D., Ph.D.](#), of the University of Massachusetts Medical School, who were given Pioneer Awards; [Manish Arora, Ph.D.](#), of the Icahn School of Medicine at Mount Sinai, who was granted a Young Innovator Award; and [Perry Hystad, Ph.D.](#), of Oregon State University, who was named an Early Independence Award winner.

- [Comprehensive Translational Science Analytics Tools for the Global Health Agenda](#), administered by NIEHS program official Caroline Dilworth, Ph.D. — Spiegelman, who is one of the few people in the world with a joint doctorate in epidemiology and biostatistics, works to advance the field of implementation science — an area of research that seeks to establish, through rigorous quantitative methods, which public health interventions, directed at achieving the same goal, are most effective in the real world.
- [tRNA \[Transfer Ribonucleic Acid\] Fragments as Transgenerational Information Carriers](#), administered by NIEHS program official Lisa Chadwick, Ph.D. — Rando, a professor of biochemistry and molecular pharmacology, focuses on one putative carrier of epigenetic information — the nucleoprotein complex known as chromatin — with the eventual goal of determining how chromatin states are established, maintained, and changed over evolution.
- [Reconstructing Fetal Toxicant Exposure and Homeostatic Disruptions](#), administered by NIEHS program official David Balshaw, Ph.D. — Arora, who holds a dual appointment in the Mount Sinai departments of preventive medicine and dentistry, conducts research focused on the application of elemental bioimaging methods, to reconstruct prenatal and early childhood metal exposures from deciduous and permanent teeth (see [story](#)).
- [PURE-AIR: A Global Assessment of Air Pollution and Cardiopulmonary Disease](#), administered by NIH Common Fund program official Ravi Basavappa, Ph.D. — Hystad, who completed graduate studies in geography and epidemiology, uses spatial exposure assessment methods to determine the chronic health effects associated with exposure to air pollution, including cardiovascular and respiratory diseases and cancer, that differ between populations in different locations.



*Pioneer Award winner Spiegelman (Photo courtesy of Harvard University)*

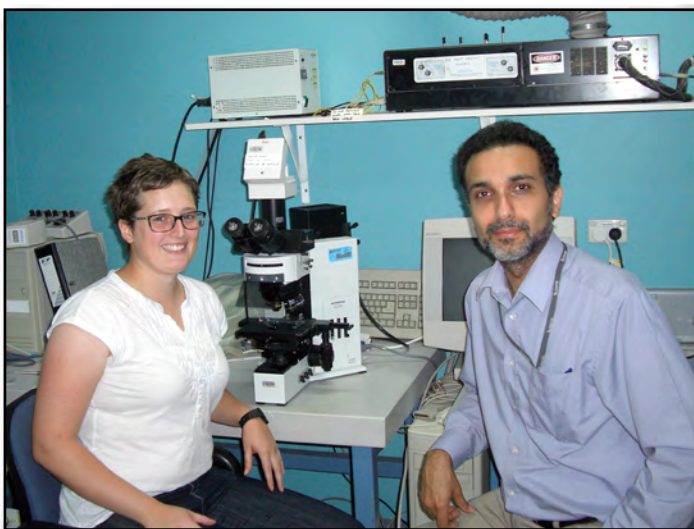


*Pioneer Award winner Rando (Photo courtesy of NIH)*

The [Pioneer Award](#), now in its 11th year, challenges investigators at all career levels to develop groundbreaking approaches that could have a significant impact on a broad area of biomedical or behavioral science.

The [New Innovator Award](#), initiative, established in 2007, supports investigators who are within 10 years of their terminal degree or clinical residency, who have not yet received a research project grant or equivalent NIH grant, to conduct unusually innovative research.

The [Early Independence Award](#), with the first awards given in 2011, provides an opportunity for exceptional junior scientists who have recently received their doctoral degree or finished medical residency to skip traditional post-doctoral training and move immediately into independent research positions.



*New Innovator Award winner Arora, right, with postdoctoral trainee Christine Austin, Ph.D., in his lab (Photo courtesy of Manish Aurora)*



*Early Independence Award winner Hystad (Photo courtesy of Perry Hystad)*

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## **NIEHS joins WHO Chemical Risk Assessment Network meeting**

*By Tara Failey*

According to the World Health Organization (WHO), more than 25 percent of the global burden of disease is linked to environmental factors. With support from NIEHS, the organization held its first [Chemical Risk Assessment Network](#) meeting Oct. 8-10 in Paris, to explore and address the public health risks posed by toxic chemicals.

The meeting was hosted by the French Agency for Food, Environmental, and Occupational Health and Safety, and attendees represented more than 55 chemical risk assessment institutions from 29 countries.

[Christopher Weis, Ph.D.](#), senior advisor and toxicology liaison for the NIEHS Office of the Director, was elected to serve as a meeting co-chair by network members.



The production and use of chemicals continues to increase worldwide, making it essential to better evaluate, and minimize, exposure to toxic chemicals,” explained Weis. “This global network will join forces to fine-tune chemical risk assessment, working to safeguard human health.”

### Keeping health at the forefront

Representatives of agencies, academic groups, and nongovernmental organizations, at the meeting, explored a variety of risk assessment challenges. These included identification of emerging risks, characterization of uncertainty in risk assessment, means to scale up capacity building, and establishment of a common understanding of systematic literature review of toxicological data.

The meeting’s keynote speaker was Kenneth Olden, Ph.D., former NIEHS director and current director of the Environmental Protection Agency National Center for Environmental Assessment. Olden reminded the audience that even though risk assessments can be highly technical in terms of methodology, assessors should keep their activities focused on public health applications. Using the epigenome as an example, he outlined how environmental justice and socioeconomic status considerations can be factored into models and recommendations.

Joining Olden and Weis was Christopher Portier, Ph.D., former director of the NIEHS Office of Risk Assessment Research, who discussed the importance of systematic review for public health decision-making.

### Identifying key challenges and opportunities for collaboration

Attendees found that interest in the health impacts of hydrofracturing and coordinating training needs crosses international boundaries. Working groups developed collaborative plans to address research in biomonitoring, identify high priority research and method development needs, increase and coordinate training efforts for risk assessors, and establish communication between participants.

Speakers from developing countries outlined some of their key struggles in risk assessment and regulation, including limited data relevant to actual exposures in their countries, and the unique climactic environments of many small island countries. Through breakout sessions and informal meetings, many attendees from developing countries received support, information, and additional data sources, from those who had conducted similar research elsewhere in the world.



*Weis, right, joined Sam Adu-Kumi, Ph.D., of the Ghana Environmental Protection Agency, during a break in the meeting. (Photo courtesy of Tara Failey)*



*Back, from left, Olden, Portier, and Weis gathered with Carolyn Vickers, front center; WHO International Programme on Chemical Safety representative. (Photo courtesy of Tara Failey)*

“As we heard about the needs of developing countries, the need for dialogue and collaboration among network members became acutely apparent,” said Weis. “The work of NIEHS is extremely important, not just for our own populations, but for other agencies, countries, and researchers around the world. We are extremely excited to be a part of this network, and hope that NIEHS can learn about unique issues in environmental health, as well as provide benefit to participants.”

(Tara Failey is a communication specialist with MDB Inc., contractor for the NIEHS Division of Extramural Research and Training.)

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## Research!America honors Olden for advocacy

*By Eddy Ball*

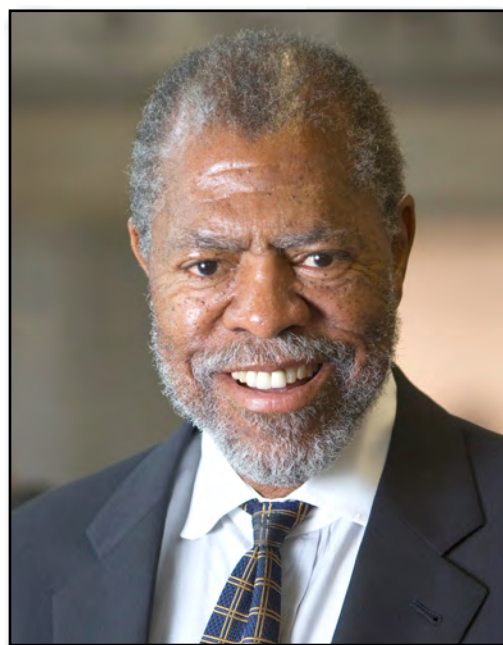
Next spring, NIEHS and National Toxicology Program (NTP) Director Emeritus Kenneth Olden, Ph.D., will be one of five people honored with a 2015 Research!America Advocacy Award. The Society for Neuroscience, which has a number of members who are NIEHS and NTP scientists, will also be recognized at the organization’s 19th annual Advocacy Awards Dinner March 11, 2015 in Washington, D.C.



[Olden](#) will be in good company when he accepts the Raymond and Beverly Sackler Award for Sustained National Leadership. “The [awards] dinner is a high-level gathering of research leaders, attended by the nation’s most influential and esteemed individuals in science, health and medical research, advocacy, business, the media, and government,” the Research!America website explains.

Along with Olden, [2015 Advocacy Awards](#) go to ABC’s “Good Morning America” anchor Robin Roberts; Michael Milken, founder of the Milken Institute and FasterCures; and David Van Andel, chairman and CEO, and George Vande Woude, Ph.D., founding research director of the Van Andel Institute.

Past winners include two Nobel laureates; actors Michael Fox and Glenn Close; former U.S. Surgeon General David Satcher, M.D., Ph.D.; public broadcasting stars Dianne Rehm and Charlie Rose; high profile politicians; and well-known nonprofits and research institutes.



*Olden during his tenure as founding dean of the CUNY School of Public Health at Hunter College (Photo courtesy of CUNY)*

### From the bench to the ranks of leadership

Trained as a cancer biologist, Olden was the second longest serving director in the history of NIEHS and NTP, from his appointment in 1991 to his return to full-time research at NIEHS in 2005. His tenure transformed the institute, as he championed environmental justice and community engagement. Because of his initiatives during that time and his work since, Research!America notes, “He is considered to be the strongest champion of community-based participatory research in the U.S.”

In 2008, The City University of New York (CUNY) selected him to be founding dean of the School of Public Health at Hunter College. Three years later, with his mission accomplished, Olden accepted the appointment to his current position as [director](#) of the U.S. Environmental Protection Agency National Center for Environmental Assessment.

Although he now works in the Washington area, Olden has maintained his ties with scientists in the North Carolina Triangle area and the many friends he made during his tenure at NIEHS. Since leaving, he has often shared the podium with NIEHS and NTP Director Linda Birnbaum, Ph.D., and other high-profile scientists from the institute.

Olden has been honored numerous times with prestigious awards, appointments, and honorary degrees, for his decades of service toward improving public health nationally and globally.

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## Bioregional planning to improve public and environmental health

*By Carol Kelly*

Disease doesn't stop at national boundaries, presenting unique international challenges. A new framework, called One Bioregion/One Health, provides an approach to transboundary regional planning that considers relationships between people and nature in the quest for healthier living spaces.

Proposed by researchers in California and Mexico and funded in part by NIEHS, the framework merges regional planning and ecosystem management as a way to improve public and environmental health. The scientists presented their proposal in an [article](#) published in the journal *Global Society*.

"Our health is affected by environmental exposures, stress, diet, urban design, and behavior," said Keith Pezzoli, Ph.D., lead author of the study and director of the Urban Studies and Planning Program at the University of California, San Diego (UCSD). "We can't think about health on just one side of the border because animals, sick people, and pollutants move back and forth," he said.

### Tracing the One Bioregion/One Health concept

A bioregion is a territory that is socially and culturally defined by its people rather than borders on a map. Bioregions are shaped by global trends, including climate change, food and water issues, economic crisis, large-scale natural disasters, and widespread increases in preventable diseases.

The One Health concept acknowledges that human health is interconnected and dependent on the health of animals and the environment. One Health is viewed by organizations such as the U.S. Centers for Disease Control and the World Bank as a way to respond to a range of emerging and existing disease threats, such as drug-resistant tuberculosis.



*"Creating a sustainable and resilient community, even across a national border, is possible by fostering investment in natural resources, rooted livelihoods, and institutions," said Pezzoli. (Photo courtesy of UCSD)*



Combining these concepts, One Bioregion/One Health is a modern approach to enable integrative, civically-engaged research to create solutions to problems, according to Pezzoli.

### Supporting ecological restoration

The authors recommend using the One Bioregion/One Health approach for ecological restoration in metropolitan areas with urban sprawl, such as those found along the United States-Mexico border. From the Pacific Ocean to the Gulf of Mexico, about 15 million people live along this increasingly urbanized border region, say the authors. Within this wide territory, the NIEHS-funded researchers at the UCSD [Superfund Research Center](#), along with partner organizations, are conducting a One Bioregion/One Health project using this approach in the San Diego-Tijuana region. One of their goals is to develop and maintain a transboundary geographic information system to aid regional decision making.

“We are joined with Mexico through the Tijuana River watershed,” said Pezzoli, who is also affiliated with the UCSD Superfund Research Center. “We are in it together because of land, buildings, and streets, but also from a health perspective.”

### Improving public health

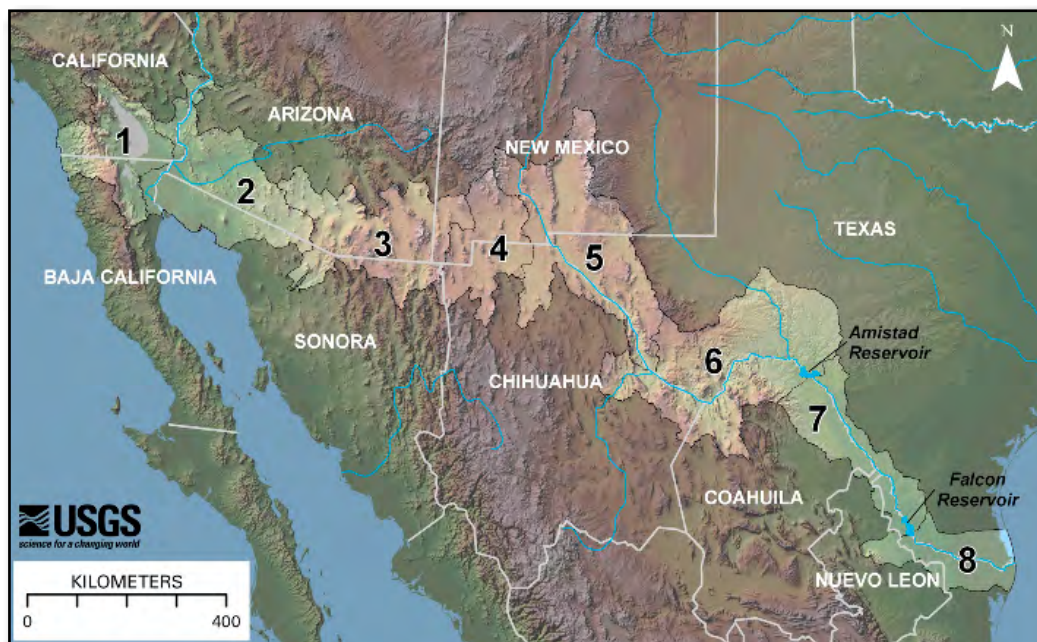
To implement the One Bioregion/One Health framework and achieve a healthy cross-border region, public health professionals need training in global health diplomacy and cooperation, according to the researchers.

They also suggest that universities, through multidisciplinary programs like the Superfund Research Center, can integrate community engagement and research translation into the efforts. In the context of ecological restoration, this cooperation and engagement is essential to the creation of healthier living spaces in a bioregion, say the authors.

*Citation:* [Pezzoli K, Kozo J, Ferran K, Wooten W, Gomez GR, Al-Delaimy WK. 2014. One Bioregion/One Health: An Integrative Narrative for Transboundary Planning along the US–Mexico Border. Global Society 28\(4\): 419.](#)

(Carol Kelly is a health and science writer with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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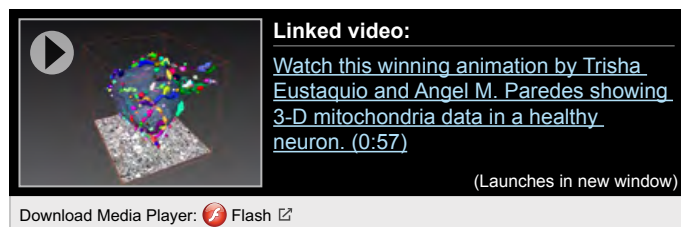


*The U.S. Geological Survey defines eight health initiative regions along the U.S.–Mexico border. (Map courtesy of U.S. Geological Survey)*

# Annual FASEB BioArt awards include NIEHS grantee

By Kelly Lenox

Each year, the Federation for American Societies for Experimental Biology (FASEB) holds a contest to find captivating images from cutting edge research. The 2014 winners were announced Oct. 7, and the entry by an NIEHS grantee and his colleagues was named among the 10 winning images. Two videos were also selected.



*"I am a big supporter of making science more accessible to the public, so I'm happy to be part of the effort FASEB is putting into that," Tolun said. (Photo courtesy of Tolun)*

## Model of DNA annealing

NIEHS grantee Jack Griffith, Ph.D., of the University of North Carolina at Chapel Hill Lineberger Comprehensive Cancer Center and the Department of Microbiology and Immunology, was the lead researcher on the project for which the image was originally generated. As part of a study published in the journal Nucleic Acids Research, the scientists presented the first 3-D reconstruction of a DNA-protein complex formed by a protein called infected cell protein 8 (ICP8), which is encoded by herpes simplex virus 1.

The winning image, prepared by Gokhan Tolun, Ph.D., who created the image while working in Griffith's lab, represents one of the two models the authors hypothesized as the mechanism by which the single-strand DNA forms a double-strand molecule. "The detail which Tolun was able to deduce provides a new view of how such large protein machines can facilitate DNA annealing and recombination," said Griffith. "This is a central goal of our funding from the NIEHS." In addition to NIEHS, the National Cancer Institute and National Institute of General Medical Sciences provided support for the research.



*Besides his notable work in the lab, Griffith is also an avid pilot, shown here with his Piper Cub. (Photo courtesy of Jack Griffith)*

## Communicating science through art

Tolun, now a postdoctoral fellow at the National Institute of Arthritis and Musculoskeletal and Skin Diseases, was the study's lead author. "The image [he] created takes advantage of both his skill in computer image reconstructions and his serious, personal hobby of photography, blending the science with a strong visual impact," said Griffith.

Tolun said he differs from scientists who usually consider preparing finely rendered figures as an afterthought. “After spending years doing the research, spending a bit more time to make that science more attractive and presentable is not only the fun part of science, but also serves the scientific community by reaching out to scientists in other areas and to the general public,” Tolun explained.

While working in Griffith’s lab as a postdoctoral fellow, Tolun found electron microscopy images prepared earlier by Alexander Makhov, Ph.D., of the University of Pittsburgh School of Medicine, another of the paper’s authors. “I told Dr. Griffith that I wanted to reconstruct these images in 3-D,” Tolun said. “He supported me to the fullest extent, and I will always be grateful to him for that.” Because the lab did not specialize in structural biology, that meant Tolun had to master both this new field and specialized scientific software packages used to determine the 3-D structures of the biological complexes.

“Given that seeing is believing,” Tolun said, “we scientists would be doing a disservice to ourselves if we did not spend some of our time making attractive-looking images to better convey our findings, proposed models, and conclusions.”

*Citation:* Tolun G, Makhov AM, Ludtke SJ, Griffith JD. 2013. Details of ssDNA annealing revealed by an HSV-1 ICP8-ssDNA binary complex. *Nucleic Acids Res.* Jun 41(11):5927-5937.

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## NIEHS fellow begins career in biopharma

*By Deepa Singh*

Research fellow Raj Gosavi, Ph.D., began a new position Sept. 29 as a bioanalytical and formulation scientist at KBI Biopharma. Gosavi is involved in characterization and stability studies of investigational new drugs that will undergo clinical testing.

Based in Durham, North Carolina, KBI Biopharma is a contract research organization that helps a range of clients, including emerging and established biopharmaceutical companies, by providing support in protein characterization, formulation, process design and development, and manufacturing.

### Well-rounded training

Gosavi obtained his Ph.D. in chemical engineering for studying the effects of additives on protein solubility and nucleation of protein crystals. His graduate work introduced him to the field of protein crystallization, and in 2008, he joined the NIEHS Collaborative X-ray Crystallography Group, headed by Lars Pedersen, Ph.D. In Pedersen’s lab, Gosavi was involved in structural characterization of several proteins, such as allergens, as well as DNA repair and hormone regulating enzymes.



*Gosavi credited Tammy Collins, Ph.D., director of the NIEHS Office of Fellows’ Career Development, for offering a wealth of resources in improving resumes and job presentations to best suit the job requirements. (Photo courtesy of Steve McCaw)*



“My move to structural biology was intended to help find a career in the biopharmaceutical industry, and the training in Pedersen’s lab allowed me to move in my desired direction,” Gosavi said.

“I am really excited for Raj and looking forward to watching him advance in his new career,” said Pedersen.

### Career resources provided by NIEHS

Gosavi credited the numerous resources and networking opportunities available to fellows at NIEHS. Working in a collaborative lab allowed Gosavi to collaborate with several other labs in the institute and required him to handle multiple projects at one time.

Gosavi highlighted the value of his roles as chair of the NIEHS Trainees Assembly Steering Committee in 2010 and as co-chair of the 2010 NIEHS Biomedical Career Fair. “These experiences provided me valuable leadership and teamwork qualities, and helped build a professional network that was extremely helpful during the job search,” he said.

Of his current adventure, Gosavi remarked, “To be part of a team that helps in developing better medicines is a rewarding and motivating experience in itself.”

(Deepa Singh, Ph.D., is a visiting fellow in the NIEHS Mechanisms of Mutation Group.)

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*“There is probably nothing more rewarding as a supervisor than when your postdoc gets a job that they are really excited about,” said Pedersen. “It’s very encouraging to know that the skill sets postdocs obtain at NIEHS are desired by industry, including local companies, allow for easy transition without uprooting families.” (Photo courtesy of Steve McCaw)*

## Taking science to a wider audience at NIEHS

*By Suchandra Bhattacharjee*

Lectures on scientific research and discoveries, which can cover subjects from epidemiology to sequencing DNA, can be difficult for a general audience to understand. At NIEHS, the nonscientific workforce is an invaluable part of the research process, and individual staff members often have an enormous curiosity about science.

The new internal NIEHS series, Big Picture, Small Talk, grew out of a desire to present scientific information to nonscientific staff. Abee Boyles, Ph.D., health scientist with the National Toxicology Program, leads a committee organizing the new series.

Opening the first talk Oct. 1, Boyles asked, “Do you want to learn how science at NIEHS supports our mission to discover how the environment affects people in order to promote healthy lives? Do you know how your day-to-day work supports the mission?”

John Schelp, from the NIEHS Office of Science Education and Diversity, followed with a presentation, “NIEHS Overview and Research Highlights.” He pointed out the importance of the National Institutes of Health, the NIEHS reporting agency, which supports a staggering 90 percent of medical and biomedical research in the U.S. Schelp also highlighted the role of NIEHS in the development of Research Triangle Park, North Carolina, and how the institute supports environmental studies to shed further light on its slogan, “Your Environment. Your Health.”

## Grass roots and cross-divisional

The grassroots initiative for the program had cross-divisional inspiration. The idea was first suggested during a 2013 NIEHS Leadership Development program, with further development at the March flash mentoring session (see [story](#)). During these events, staff in the NIEHS Office of Management expressed a desire to better understand the science they support by their work.

NIEHS scientists have found few avenues to present their work to the nonscientific community at NIEHS. Presentations to the general public often take place outside the institute. The committee hopes to encourage scientific staff to hone their communication skills by presenting research from a big picture perspective, and by participating in talks outside of their area of research.

The series aims to broaden the audience for internal scientific talks, and include interactive formats to help bolster networking between scientific and nonscientific staff, and across divisions. The series name, “Big Picture, Small Talk,” was coined by Gary Bird, Ph.D., staff scientist in the NIEHS Calcium Regulation Group. The organizing committee, headed by Boyles and including personnel from all divisions in the institute, is actively working to line up speakers for the series.



*“One of the inspirations [of the series] was a staff member in the Office of Acquisitions who wanted to understand more about the science behind the things she was being asked to buy,” said Boyles. (Photo courtesy of Steve McCaw)*

## Upcoming Big Picture, Small Talk

### **Environmental Accidents: What Role Is NIEHS Playing?**

Tuesday, Nov. 18, 2:00 p.m.

Building 101, Executive Conference Room

Richard Kwok, Ph.D., Epidemiology Branch

Scott Auerbach, Ph.D., Biomolecular Screening Branch

### **How Therapeutic Drugs and Nasty Chemicals Move Around Your Body**

Wednesday, Dec. 3, 2:30 p.m.

Building 101, F193

David Miller, Ph.D., Signal Transduction Laboratory

### **Planned for 2015**

#### **The Environment and the Brain: Alzheimer Disease, Autism, Addiction, etc.**

Jerry Yakel, Ph.D., Neurobiology Laboratory

#### **What Is Fracking? Why Is It Always in the News?**

Aubrey Miller, M.D., Office of the Director

#### **Animal Research at NIEHS**

Terry Blankenship-Paris, D.V.M., Comparative Medicine Branch



*Schelp's overview was packed with fascinating tidbits of NIEHS history and growth, followed by a lively discussion among participants. (Photo courtesy of Steve McCaw)*

(Suchandra Bhattacharjee, Ph.D., is a special volunteer in the NIEHS Free Radical Metabolism Group.)

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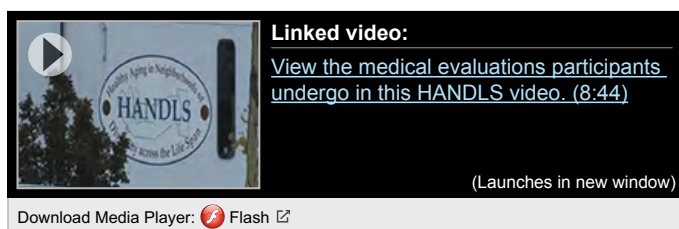
# Clinical Feature

## NIA study focuses on health disparities

By Robin Arnette

The NIEHS Office of Human Research Compliance (OHRC) continued its seminar series Oct. 15 with a discussion of a study that experienced success in recruiting and retaining participants for clinical research.

Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) is a 20-year population-based health disparities study of residents living in Baltimore, Maryland (see side bar). An unprecedented 91 percent of participants who signed up for the study took part in the second wave of medical evaluations that occurred a few years later.



HANDLS is sponsored by the National Institute on Aging (NIA), and owes its existence to its two NIA creators — Deputy Scientific Director Michele Evans, M.D., and lead researcher Alan Zonderman, Ph.D. Evans and HANDLS clinical study manager Jennifer Norbeck were invited to NIEHS to talk about the challenges of recruiting special populations and discuss study results.

### Earning trust

Norbeck spoke first and described the barriers she and the team had to overcome to recruit and retain the target population — a socioeconomically diverse sample of young to middle-aged African-Americans and Caucasians in Baltimore. Based on scientific literature, the team identified several barriers to participation. Mistrust of government and research, and transportation issues prompted HANDLS staff to conduct the study off-site and develop community partnerships during the planning phase.

The first step in establishing a physical presence in the community was to follow the National Health and Nutrition Examination Survey (NHANES) model of mobile examination centers. The team designed and procured three medical research vehicles (MRVs) — a 56-foot

### The HANDLS protocol

HANDLS staff selected one or two individuals per household, using a computer-generated probability method, which yielded a representative sample from Baltimore. The study has several exclusion criteria, such as pregnancy or drug and alcohol abuse. To participate in the study, residents had to be 30 to 64 years old, be able to give informed consent, and have photo identification.

While compensation was important for some, flexible scheduling was critical during the first wave of the study. The team successfully recruited 3,720 participants.



Evans uses her skills as an internist and medical oncologist in her position as deputy scientific director at NIA. (Photo courtesy of Steve McCaw)



semi-customized trailer with three testing areas, called MRV-1; a 40-foot self-propelled truck with three rooms for obtaining consent and cognitive testing, called MRV-2; and a third smaller vehicle used exclusively for specimen collection, called MRV-3.

After eliminating the need for residents to travel to a testing site, HANDLS staff had to earn the trust of people living in the area. Norbeck said the study was much better received by residents who had seen the MRVs in the neighborhood and had gotten a letter about participating.

“We also posted flyers, attended community events, placed ads in local newspapers and community association newsletters, and created community advisory boards,” Norbeck said. “We did all this before we knocked on any doors.”

### Searching for the cause of health disparities

Evans began her portion of the seminar by explaining the rationale for HANDLS. She said residents in some Baltimore neighborhoods have longer life expectancy than others. Affluent Roland Park has a life expectancy of 83 years, while Hollins Market, which has a majority of those with lower socioeconomic status, is 63 years.

Evans said this surprisingly low number compares to life expectancy in the U.S. in 1940, or Bangladesh and Pakistan today. She and Zonderman wondered if there was biologic damage associated with the living conditions in selected neighborhoods in Baltimore.

“We wanted to know if environment, occupation, race, or lifestyle was driving these differences,” Evans said. “How do these social determinants of health cause health disparities?”

African-Americans in these neighborhoods had a higher incidence of chronic kidney disease, but since Caucasians also suffered with the disease, race was not a factor. HANDLS staff, along with Deidra Crews, M.D., of Johns Hopkins School of Medicine, found that poverty was an important risk factor only in African-Americans, suggesting that environmental factors associated with poverty posed a specific risk for chronic kidney disease among African-Americans.

Working with collaborators at Massachusetts General Hospital, the HANDLS team wanted to understand why African-Americans exhibited low vitamin D levels, but didn’t display symptoms of vitamin D deficiency. They found that some versions of the protein are more abundant in African-Americans than European-Americans and have different binding affinities for vitamin D (see [text box](#)).

HANDLS serves the community by providing comprehensive medical examination, clinical labs, and health education to those who otherwise could not afford them. It also contributes to the well-being of its participants, by sending lab results to them by mail and sharing the information with their doctors.



*Norbeck has a master’s degree in social work. This training was exactly what Evans was looking for when she asked Norbeck to join the HANDLS team in 2003. (Photo courtesy of Steve McCaw)*



*NIEHS OHRC Director Joan Packerham, Ph.D., presented Evans and Norbeck with a poster of the announcement for their seminar. (Photo courtesy of Steve McCaw)*

## Low vitamin D

Since physicians measure the amount of vitamin D bound to a binding protein, HANDLS researchers examined the genotype of vitamin D binding protein that binds 85-90 percent of total circulating 25-hydroxyvitamin D in African-American and Caucasian HANDLS participants.

The researchers found that low total 25-hydroxyvitamin D levels likely do not indicate true vitamin D deficiency when vitamin D binding protein levels are also low, as with many African-Americans. Estimated bioavailable 25-hydroxyvitamin D levels among African-Americans and Caucasians were comparable, suggesting that perhaps a new test for vitamin D deficiency should assess the amount of free or bioavailable vitamin D and assess the vitamin D binding genotype of individuals.

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# Science Notebook


## Distinguished lecture explores contradictory role of Hedgehog signaling

By Jordan St Charles

In his Sept. 26 distinguished lecture, “Hedgehog signaling in organ homeostasis and malignancy,” Philip Beachy, Ph.D., described a role of Hedgehog signaling in preventing epithelial cancer in the bladder and pancreas, which contradicts the pro-cancer role that Hedgehog signaling has in the development of medulloblastomas and basal cell carcinomas. Hedgehog is the name of a particular signaling molecule that binds with a target protein in a biochemical process known as the Hedgehog pathway.

Beachy was hosted by Traci Hall, Ph.D., head of the NIEHS Macromolecular Structure Group, and Humphrey Hung-Chang Yao, Ph.D., head of the Reproductive Developmental Biology group. “His work is a must read for everyone who studies developmental biology,” said Yao in his introduction.



A professor of biochemistry and developmental biology in the Stanford School of Medicine, [Beachy](#) has been a member of the National Academy of Sciences since 2002. His lab focuses on the function of Hedgehog proteins in morphogenesis and injury repair. Describing the diverse roles of Hedgehog signaling, Beachy’s topics ranged from its importance in embryonic development to a newly understood role in restraining proliferation of invasive carcinomas.



**Linked video:**  
[Watch Beachy in this Stanford video, discussing the role of Hedgehog signaling in cancer, through minute 59:12 \(1:54:06\)](#)

Philip Beachy, Ph.D.  
Ernest & Amelia Gallo Professor  
Stanford School of Medicine

(Launches in new window)

Download Media Player:  Flash 

### Hedgehog in development

Traditional studies of the Hedgehog pathway have focused on its role in embryo development. Disruption of the pathway during development can cause problems such as a rare birth defect called cyclopia, in which embryos lack midline structures of the face and brain and consequently develop only one eye and nostril.



*Beachy discussed new areas of research, including the role of Hedgehog signaling in processes in which the stroma actually restrains tumor growth. (Photo courtesy of Steve McCaw)*



*“Beachy made the groundbreaking discovery of the Hedgehog signaling pathway and molecular regulation in *Drosophila*,” said Yao, when introducing Beachy. “I have known his work for a long time and it’s a great honor to have him here in person.” (Photo courtesy of Steve McCaw)*



In the Hedgehog pathway, the Hedgehog protein binds to a receptor known as Patched, activating an important downstream protein known as Smoothened and allowing important downstream events to take place. In the absence of Hedgehog, Patched inhibits the activity of Smoothened, preventing activation.

### **Hedgehog and bladder infections**

In addition to its role in development, Hedgehog signaling is important for the recovery of organs following damage. Beachy described his work examining the Hedgehog role in bladder recovery from urinary tract infections.

When bacteria are introduced into the bladder, apoptosis, or cell death, occurs, followed by exfoliation of the top layer of cells. Basal cells, located below the top layer of cells, produce the Hedgehog signal in response to the bacterial damage. The Hedgehog signal then causes factors to be expressed that lead to cell differentiation, restoring function within the bladder tissue.

Beachy reported that this feedback system functions in many tissue systems and ruminated on possible reasons that the system evolved in this manner. “The epithelia in all of our organs are the tissue layer that takes the hit,” he said. “If we breathe or eat something bad, it’s the lung or intestinal epithelium that is affected and the underlying stromal cells are not injured.”

### **Hedgehog signaling and epithelial cancer**

Beachy’s lab has also studied the role of Hedgehog signaling in urothelial cancer development. Studying the origin of the cancer and whether cancer cells are derived from stem cells, the scientists were able to show that the basal cells that express Hedgehog can give rise to cancer cells. They further showed that if these cells are destroyed, cancer does not form, indicating that in this model, invasive carcinoma arises from basal cells.

However, when the researchers examined the cancer cells after they had become invasive, they found that these cells no longer expressed the Hedgehog protein. Further experiments indicated that Hedgehog signaling to the stroma causes release of pro-differentiation factors from stromal cells that can restrain tumor growth and progression.



*Birnbaum listened closely as Beachy outlined new studies into drugs that may block carcinoma development. (Photo courtesy of Steve McCaw)*



*Beachy drew a diverse crowd including from left, Benjamin Scruggs, Ph.D., of the Chromatin and Gene Expression Group, Natacha Steinckwich-Besancon, of the Calcium Regulation Group, Doug Bell, Ph.D., head of the Environmental Genomics Group, and Steve Kleeberger, Ph.D., head of the Environmental Genetics Group. (Photo courtesy of Steve McCaw)*



*The Reproductive Medicine Group was well represented, including from left, group lead Carmen Williams, Ph.D., Wendy Jefferson, Ph.D., biologist, and Alisa Suen, visiting predoctoral fellow. (Photo courtesy of Steve McCaw)*

This is very different from other cancers, such as medulloblastoma, in which Hedgehog activation within the primary cells of the tumor has been shown to promote cancer growth. Beachy suggested that these differences should be considered during treatment. “This suggests that the Hedgehog pathway and its antagonists have to be handled with care and patients should be monitored very closely,” he said.

(Jordan St Charles, Ph.D., is an Intramural Research and Training Award fellow in the NIEHS DNA Replication Fidelity Group.)

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## Distinguished lecture examines the rise of allergic disease

By Robin Arnette

Researchers are not sure what is behind the emergence of allergic diseases, but allergist Thomas Platts-Mills, M.D., Ph.D., has several theories about their origin. Platts-Mills has been treating allergy sufferers for more than 30 years, and believes these illnesses are the result of changes in human behavior.

During an Oct. 14 NIEHS Distinguished Lecture, “Epidemics of allergic disease 1870-2010: hay fever, asthma, peanut allergy and now delayed anaphylaxis to red meat,” he discussed the possible roots of four allergic diseases that have surfaced during the modern era.



**Linked video:**  
[Platts-Mills characterized the processes involved in food allergies in this 2013 video. \(20:46\)](#)

(Launches in new window)

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### The summer sneeze

Although Blackley found the connection between pollen and hay fever, another British physician was actually the first to describe the condition. John Bostock Jr., M.D., presented a study to colleagues in 1819, in which he described the nose and throat inflammation, called catarrh, he experienced every summer. Bostock coined the phrase *catarrhus aestivus*, or “summer catarrh,” in a paper published in 1828. Some of his contemporaries thought the ailment was the result of smelling new hay — hence, the name hay fever.

### The pollen wars

Platts-Mills began his talk with Charles Blackley, M.D., the British scientist who discovered the mechanism behind hay fever. Blackley performed skin tests and calculated the rate of pollen being inhaled to prove that pollen caused hay fever. He published his findings in 1873 (see side bar).

Platts-Mills said hay fever, or allergic rhinitis, occurs because the body’s immune system believes pollen grains are foreign pathogens, and mounts a powerful allergic response. He speculated that the explosion of pollen could be linked to the revolution in agriculture that followed reform of the Corn Laws in 1847. Platts-Mills clarified that the British word for wheat is corn.



*Platts-Mills is a professor of medicine, allergy, and clinical immunology at the University of Virginia School of Medicine. He is also a Fellow of the Royal Society. (Photo courtesy of Steve McCaw)*



## Pediatric asthma and the exodus indoors

While the number of hay fever cases peaked in the 1950s, Platts-Mills said childhood asthma followed a different course. He explained that doctors started seeing the first instances of childhood asthma in the 1960s, and the trend took off from there.

He believes two issues may be at play. The first is the hygiene hypothesis, which says the low incidence of childhood infections in developed countries contributes to an increased incidence of allergic diseases. The second implicates the advent of television.

“My wife can remember the moment in which someone said, ‘I’m going in to watch television,’ and that was 1954,” Platts-Mills recalled. “Now, kids can’t be persuaded to go outside.”

He surmised that warmer homes allow mites to multiply faster, exposing occupants to more of their allergens. In addition, scientists determined that people watching a screen, such as TV or a computer, stopped sighing, or taking deep breaths, compared to people who sigh unconsciously while reading. Individuals that don’t sigh regularly tend to have lungs that contract more intensely than normal to a stimulus.

## Peanuts and tree nut allergies

In the 1980s, Platts-Mills and his colleagues rarely saw children with peanut allergies in their clinic, but times have changed. A 2010 [study](#) published in the Journal of Allergy and Clinical Immunology indicated that the number of children with peanut allergies increased three-fold between 1997 and 2008.

Although the rise in peanut and tree nut allergies is harder to explain, Platts-Mills suggested that sensitization may occur through the skin. As an example, he mentioned that many Japanese women have developed sensitization to wheat after continued use of a skin cream that contained wheat.

## Carnivores beware

Members of the Platts-Mills group began research on red meat allergies after hearing about two incidents — a hunter reporting a severe allergic reaction, known as anaphylaxis, after eating red meat, and a patient dying after receiving [cetuximab](#), a medicine made of monoclonal antibodies used to treat head and neck cancers.

They knew that meat from mammals contained a carbohydrate called galactose-alpha-1,3-galactose, also known as alpha gal, but they didn’t understand why certain people were developing allergic immunoglobulin E (IgE) antibodies to it. Another scientist noticed that the pattern of cetuximab anaphylaxis in the United States resembled the pattern of Rocky Mountain spotted fever, which is spread by a tick.



*“It was a real pleasure to bring Dr. Platts-Mills to NIEHS,” said Geoffrey Mueller, Ph.D., staff scientist in the NIEHS Nuclear Magnetic Resonance Group and host of the presentation. “He was a member of my Ph.D. thesis committee at the University of Virginia.” (Photo courtesy of Steve McCaw)*



*Serena Dudek, Ph.D., standing, is head of the NIEHS Synaptic and Developmental Plasticity Group. She asked Platts-Mills whether the women that became sensitized to wheat were actually sensitive to gluten. (Photo courtesy of Steve McCaw)*



“After we developed an assay for IgE antibodies to cetuximab, we realized that someone who has never been allergic before can receive a Lone Star tick bite and become highly allergic to red meat,” Platts-Mills said. “The reaction happens 2 1/2 to six hours after the bite.”

Platts-Mills added that the expanding deer population, which carries ticks, is responsible for the upsurge in meat allergies. Changes in hunting patterns and leash laws, which prevent packs of dogs from roaming neighborhoods, no longer keep deer numbers in check.

He concluded by saying, although humans can’t predict the diseases that our actions generate, we should think more carefully about how we are impacting our environment.

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*Asthma specialist Stavros Garantziotis, M.D., is acting chief of the NIEHS Clinical Research Branch and leads the Matrix Biology Group. He wondered if there was a connection between red meat allergy and angioedema, or swelling of the skin around the mouth and lining of the throat, after a tick bite. (Photo courtesy of Steve McCaw)*

## The 13th Report on Carcinogens includes four newly reviewed substances

*By Robin Mackar*

U.S. Department of Health and Human Services Secretary Sylvia Burwell released the 13th [Report on Carcinogens](#) Oct. 2 in Washington, D.C. Four substances were newly reviewed for this edition, which brings the cumulative report to a total of 243 listings. The new substances include ortho-toluidine, 1-bromopropane, cumene, and a pentachlorophenol mixture.

The [National Toxicology Program](#) (NTP) prepares the congressionally mandated [report](#) for the Secretary. The science-based document identifies agents, substances, mixtures, or exposures in two categories — known to be a human carcinogen and reasonably anticipated to be a human carcinogen.



### One substance newly listed as a known human carcinogen

Since 1983, ortho-toluidine has been listed in the Report on Carcinogens as reasonably anticipated to be a human carcinogen. New cancer studies led NTP to reevaluate and reclassify ortho-toluidine as known to be a human carcinogen, based on studies in humans that showed it causes urinary bladder cancer. Ortho-toluidine is a synthetic chemical produced in other countries that is imported to the U.S. in high volumes by several companies. It is primarily used to make rubber chemicals, pesticides, and dyes. It is also used in some consumer and medical products.

### Three substances added as reasonably anticipated to be a human carcinogen

The chemical 1-bromopropane is a solvent widely used as a cleaner for optics, electronics, and metals, as well as a solvent for aerosol-applied adhesives, such as those used in foam cushion manufacturing. It is also used in dry cleaning and solvent sprays for aircraft maintenance. Workers in certain occupations may be more exposed to 1-bromopropane than the general population.

Cumene, a natural component of coal tar and petroleum, is used primarily to make acetone and phenol. It is also found in tobacco smoke and emissions from petroleum products. People are mainly exposed to cumene through the environment and in workplaces that use or produce cumene.

The listing of pentachlorophenol and by-products of its synthesis addresses a complex mixture of chemicals used as wood preservatives. In the U.S., pentachlorophenol has been regulated since the 1980s as a restricted-use pesticide. It is used industrially for treating utility poles, wood pilings, fence posts, and lumber or timber for construction.

### Valuable resource for prevention

“This report provides a valuable resource for health regulatory and research agencies, and it empowers the public with information people can use to reduce exposure to cancer-causing substances,” said NIEHS and NTP Director Linda Birnbaum, Ph.D.

A listing in the Report on Carcinogens does not by itself establish that a substance will cause cancer in an individual. Many factors, including the amount and duration of an exposure, and an individual’s susceptibility to a substance, influence whether a person will or will not develop cancer.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)



*Ruth Lunn, Dr.P.H., directs the NTP Office of the Report on Carcinogens, which is responsible for the scientific evaluation process and preparation of the report. (Photo courtesy of Steve McCaw)*

#### Summary of Newly Reviewed Substances

Substance	Listing Status	Description and Use
1-Bromopropane	<i>Reasonably anticipated to be a human carcinogen</i>	Used as a cleaning solvent and in spray adhesives
Cumene	<i>Reasonably anticipated to be a human carcinogen</i>	Used to make phenol and acetone, and found in fuel products and tobacco smoke
Pentachlorophenol and By-Products of Its Synthesis	<i>Reasonably anticipated to be a human carcinogen</i>	A complex mixture used as a wood preservative to treat utility poles
<i>ortho</i> -Toluidine	<i>Known to be a human carcinogen*</i>	Used to make rubber chemicals, pesticides, dyes, and medical and consumer products, and found in tobacco smoke

*\*ortho*-Toluidine was reevaluated and reclassified for the 13th Report on Carcinogens. It was previously listed as reasonably anticipated to be a human carcinogen.

# Veterinary pathology group chooses Malarkey as 2015 president-elect

*By Eddy Ball*

National Toxicology Program (NTP) Pathologist David Malarkey, D.V.M., Ph.D., was elected this summer as 2015 president-elect of the American College of Veterinary Pathologists (ACVP), an organization of board-certified specialists that has been setting the standard for veterinary pathology since 1949. The announcement from ACVP secretary-treasurer Michael Topper, D.V.M., Ph.D., appeared in the September issue of the organization's quarterly newsletter.

[Malarkey](#), who has been a diplomate of the [ACVP](#) since 1993, is the head of the NTP Pathology Group in the Cellular and Molecular Pathology Branch, which provides peer-reviewed pathology evaluations that are considered the gold-standard by regulatory agencies worldwide. His group members provide data and scientific interpretation for all toxicology and carcinogenesis studies at NTP for eventual public dissemination. The group offers specialty training positions for veterinary pathology trainees and other scientists, as well as externships for veterinary or other students.

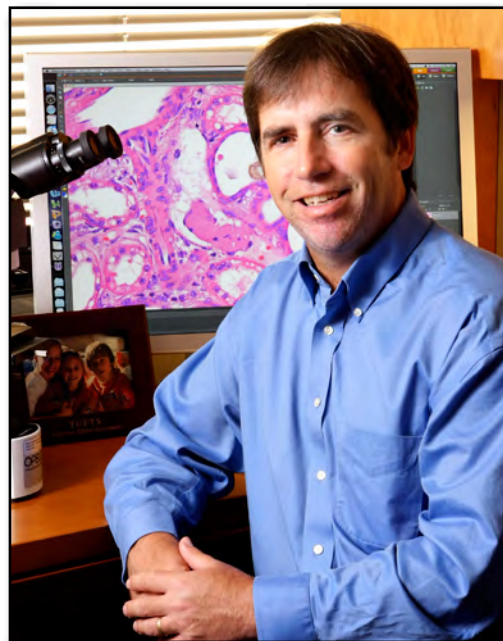
## At the head of his class

"ACVP is the largest organization of all board-certified veterinary pathologists in the world. [David's] election is a tremendous honor for NTP and NIEHS and underscores the amazing pathology leadership we are privileged to have," said [Robert Sills, D.V.M., Ph.D.](#), head of the NTP Cellular and Molecular Pathology Branch.

Malarkey, who is currently finishing his fourth year on the ACVP Council, will start his new position at the end of the ACVP annual meeting Nov. 8-12 in Atlanta, in partnership with the American Society for Investigative Pathology. He was chosen in an election with the largest turnout of voting members in the history of the organization.

As president, Malarkey will lead an elite cadre of 2,100 members, who are all board-certified pathologists. Veterinarians who successfully complete the certifying examination are accepted into the organization as diplomates. "I am honored and thrilled to lead and represent the membership," said Malarkey.

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*Malarkey was an Intramural Research Training Award fellow at NIEHS 1993-1997 and assistant professor of pathology at North Carolina State University 1997-2002 before rejoining NIEHS in 2002. (Photo courtesy of Steve McCaw)*



# Ethnic ancestry among Latinos influences asthma risk

By Ernie Hood

Researchers at the University of California, San Francisco (UCSF) and collaborators have shown that, among U.S. Latino children, the risks of developing asthma and lower lung function vary with genetic ancestry, even after adjusting for well-known social and environmental risk factors.

The [study](#) assessed asthma prevalence and lung function in 5,493 Latino children who were identified as being of Mexican, Puerto Rican, or other Latino ethnicity. “This is the largest, most comprehensive study of its kind in minority children,” said lead study scientist Esteban Burchard, M.D., a professor of bioengineering and therapeutic sciences at UCSF. Largely funded by NIEHS, the study was published online Oct. 6 in the Journal of Allergy and Clinical Immunology.

## Genetic ancestry matters

Among U.S. Latino children, asthma prevalence is highest in Puerto Ricans and lowest in Mexican-Americans. In general, Mexicans have more Native American ancestry, while Puerto Ricans have more African ancestry, with European ancestry common to both groups.

For each of the participants, the scientists used genome-wide data to estimate the proportion of African, European, and Native American ancestries. The analysis showed that for the Puerto Rican children, every 20 percent increase in African ancestry correlated with a 40 percent increase in asthma risk. Among Mexicans and other Latinos, every 20 percent increase in Native American ancestry resulted in a 43 percent decrease in the odds of developing asthma.

Even without asthma, lung function was lower among children with more African ancestry.

## Care with confounders

The scientists analyzed data from three previous independent studies. Using genotyping and sophisticated statistical methods, they were able to distinguish genetic influences on disease risk from environmental factors. The researchers found that the study results did not change when environmental or socioeconomic factors were considered, suggesting that genetic differences were the primary cause of the disparities.



*Pino-Yanes and colleagues demonstrated that disparities in asthma prevalence and lung function among Latinos can be partially explained by differences in genetic ancestry. (Photo courtesy of Sam Oh, UCSF)*



*Burchard's research has shown that, in comparison to white children, a higher percentage of minority children are not helped by inhaled asthma rescue medications. (Photo courtesy of Sam Oh, UCSF)*

“We took into account a wide variety of possible confounders that have never been considered in any other previous study of ancestry and asthma,” said Maria Pino-Yanes, Ph.D., a postdoctoral fellow in Burchard’s lab and lead author of the study. “We included exposure to air pollution in the first year of life, indicators of socioeconomic status, mother’s highest education level, child’s health insurance status, discrimination, acculturation, and variables related to secondhand smoking.”

### Clinical implications

The findings may have an immediate impact on clinical practice. Doctors currently compare lung function test results to a standard reference to determine if the patient has lung disease, such as asthma, and the severity. Results showing differences in normal lung function among Latino children of diverse genetic ancestries suggest that the diagnosis of asthma and other lung disease in these groups should be more refined than it is at present.

“We need to develop new pulmonary reference standards to predict normal lung function in Puerto Ricans, who have the highest asthma prevalence and death rates,” Burchard said. “The current method for predicting lung function in Puerto Ricans relies on reference equations derived from Mexicans or whites.”

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

*Citation:* Pino-Yanes M, Thakur N, Gignoux CR, Galanter JM, Roth LA, Eng C, Nishimura KK, Oh SS, Vora H, Huntsman S, Nguyen EA, Hu D, Drake KA, Conti DV, Moreno-Estrada A, Sandoval K, Winkler CA, Borrell LN, Lurmann F, Islam TS, Davis A, Farber HJ, Meade K, Avila PC, Serebrisky D, Bibbins-Domingo K, Lenoir MA, Ford JG, Brigino-Buenaventura E, Rodriguez-Cintron W, Thyne SM, Sen S, Rodriguez-Santana JR, Bustamante CD, Williams LK, Gilliland FD, Gauderman WJ, Kumar R, Torgerson DG, Burchard EG. 2014. Genetic ancestry influences asthma susceptibility and lung function among Latinos. *J Allergy Clin Immunol*; doi:10.1016/j.jaci.2014.07.053 [Online 6 October 2014].

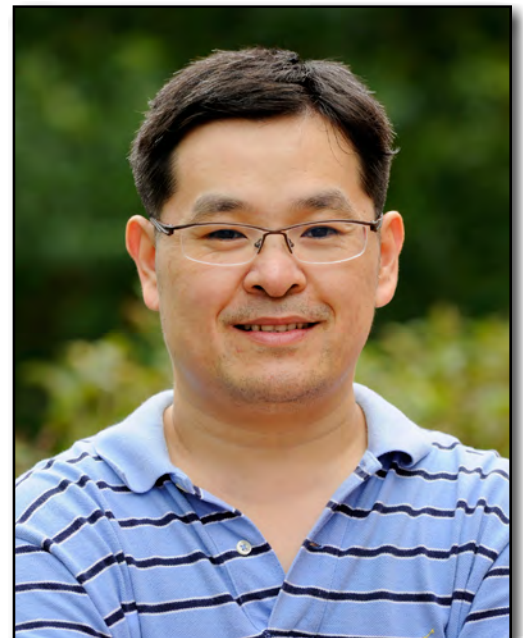
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## NIEHS scientists participate in 2014 NIH Research Festival

*By Eddy Ball*

Despite continuing limitations on travel, several NIEHS and National Toxicology Program scientists and trainees were on hand for the 2014 NIH Research Festival Sept. 22-24 in Bethesda, Maryland. In line with the [Brain Research through Advancing Innovative Neurotechnologies Initiative](#) launched in 2013, the Research Festival was organized around the theme, “The Era of the Brain.”

In addition to talks and posters by institute scientists, the 17 NIEHS trainees who won the 2015 Fellows Award for Research Excellence (FARE) travel awards (see [story](#)) were recognized Sept. 22 during the opening plenary session.



*Wang won FARE awards the last three years.  
(Photo courtesy of Steve McCaw)*

Two NIEHS FARE winners received special recognition at the festival — [Barbara Nicol, Ph.D.](#), winner of one of just three Women Scientist Advisors Committee Scholar Awards presented this year (see [story](#)), and three-time FARE winner [Qingshan Wang, M.D.](#), who made a 20-minute oral presentation on his award-winning research, as part of the Sept. 23 concurrent symposia session, “Glia: A New Frontier.”

“I congratulate Barbara and Qingshan for this recognition of their excellent work,” said William Schrader, Ph.D., NIEHS deputy scientific director and training director. “They received special travel awards from the NIEHS Office of the Scientific Director, so they can use their FARE travel awards for other professional development opportunities.”

## On the agenda

Oral presentations by NIEHS scientists:

- During the glia session, Wang discussed the study he conducted with mentor John Hong, Ph.D., “A novel therapeutic strategy for Parkinson’s disease by inhibiting microglial NADPH oxidase.”
- Also speaking in the glia session, National Toxicology Program neurobiologist and lead researcher Jean Harry, Ph.D., explored “Microglia involvement in environmentally-induced neuronal death and stimulation of hippocampal neural progenitor cells.”
- The “Stem Cells in Development and Diseases” concurrent symposia session featured a talk by lead researcher Guang Hu, Ph.D., “Transcriptional and post-transcriptional regulation of embryonic stem cell self-renewal.”

Poster presentations of NIEHS research:

- Nicol’s award-winning study, “[Sox9/ \$\beta\$ -catenin Double Knockout Mice Uncover a New Paradigm in Testis Differentiation](#),” co-authored with mentor and lead researcher Humphrey Yao, Ph.D.
- A study, “[Exposure to Indoor Allergens in Relation to Asthma: Results From the National Health and Nutrition Examination Survey \(NHANES\)](#),” by a team of respiratory biologists led by NIEHS Scientific Director Darryl Zeldin, M.D., and epidemiologist Paivi Salo, Ph.D.
- Two theoretical studies led by biostatistician and lead researcher Shyamal Peddada, Ph.D. — “[Modeling Fine Particulate Matter Along the Gulf Coast From the Deepwater Horizon Oil Spill](#),” with co-author and postdoctoral fellow Casey Jelsema, Ph.D., who attended the festival; and “[Analysis of Composition of Microbiomes \(ANCOM\): A Novel Method for Studying Microbial Composition](#),” with a team of researchers from several institutions.

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*Nicol was selected for a Women Scientist Advisors Committee Scholar Award from this year’s pool of 113 women scientist FARE winners. (Photo courtesy of Steve McCaw)*



# NCSOT fall meeting highlights “Hot Topics in Toxicology”

*By Deacquinta Diggs*

The North Carolina chapter of the Society of Toxicology (NCSOT) held its annual fall meeting Oct. 9 in the Rodbell Auditorium at NIEHS.

Chapter president and RTI International nanotoxicologist [Christie Sayes, Ph.D.](#), opened the meeting, which featured talks on hydrofracturing, coal fly ash, and e-cigarettes, by describing the professional responsibility of members to stay abreast of new developments and hot topics in toxicology.

“We need to educate ourselves and educate our peers on how we can have successful positive conversations with our friends, neighbors, and colleagues on these areas of toxicology and environmental health that are hitting the news,” Sayes stated.

## Postdoctoral fellows honored for quality research

The President’s Awards for Research Competition (PARC) were also presented to postdoctoral fellows who submitted abstracts to the competition. The third place winners were Yong Ho Kim, Ph.D. and Rui Yu, Ph.D. The second place winner was Yongquan Lai, Ph.D., and first place went to Samantha Snow, Ph.D., who gave an oral presentation as part of her prize.

Snow discussed the connection between ozone exposures and the metabolic diseases diabetes and obesity. “A risk factor for metabolic disease includes ambient air pollution,” Snow said. “There is a link between fine particulate matter and prevalence of diabetes in America.”

## Fracking, coal ash, and e-cigarettes — emerging public health concerns

University of Pennsylvania pharmacologist [Trevor Penning, Ph.D.](#), discussed hydraulic fracturing (hydrofracking). He focused on the rapid growth of hydrofracking in Pennsylvania, where the Marcellus Shale, a rich source of natural gas, takes up about half of the state’s land mass.

“I think this industry is here to stay, but it needs to be done safely,” said Penning. Health concerns include water contamination from drilling and air pollution from diesel truck exhaust. “I think there are ways to improve the technology,” said Penning.



*Sayes opened the fall meeting on hot topics in toxicology by noting the chapter’s growth to 411 members, making it one of the largest and most active in the U.S. (Photo courtesy of Steve McCaw)*



*Kim, right, a UNC postdoc working at the U.S. Environmental Protection Agency (EPA), received \$100 as part of his third place finish in the PARC Award competition. (Photo courtesy of Steve McCaw)*

North Carolina State University environmental toxicologist [David Buchwalter, Ph.D.](#), explored the growing controversy over coal ash in North Carolina waterways. “The more stuff we keep out of air, the more we are creating waste streams that pollute water,” he explained.

Buchwalter’s focus was the wet storage of ash. Once ash is released from power plants and makes contact with water, he said, trace elements are released almost immediately, resulting in water contamination. “Arsenic and selenium are the two things we focus on the most in terms of ecological human health concerns,” said Buchwalter. He concluded that water contamination is preventable, but very costly to remediate.

University of North Carolina at Chapel Hill (UNC) respiratory biologist [Ilona Jaspers, Ph.D.](#), discussed the health concerns of the increasingly popular e-cigarettes. She explained that there is little knowledge about the long-term health effects of toxic compounds used in this new method of nicotine delivery. She also pointed out that e-cigarettes are not currently regulated by the U.S. Food and Drug Administration (FDA).

“We have absolutely no idea about flavor toxicity,” she said, pointing to the more than 7,000 flavors now on the market for e-cigarettes. Because little data are available, animal and *in vitro* models are needed to study the short- and long-term effects of using e-cigarettes.

NCSOT councilor and NIEHS postdoctoral fellow, Jason Stanko, Ph.D., secured sponsorship for the meeting from Charles River Laboratories, The Society of Toxicology, The Hamner Institutes for Health Sciences, and Burroughs Welcome Fund.

(Deacqunita Diggs, Ph.D., is a National Health and Environmental Effects Research Laboratory postdoctoral fellow at the U.S. Environmental Protection Agency in Research Triangle Park, North Carolina)



*Yu, a postdoc at UNC, tied for third place. (Photo courtesy of Steve McCaw)*



*The second place PARC award went to Li, a postdoc at UNC, who received \$200 as part of his prize. (Photo courtesy of Steve McCaw)*



*Winning the first place PARC award earned Snow a cash prize of \$300 and the privilege of making an oral presentation on her research. She is an Oak Ridge Institute for Science and Education postdoc at EPA. (Photo courtesy of Steve McCaw)*





*Penning, an NIEHS grantee, underscored the seriousness of hydrofracking as a public health concern, but he also managed to enjoy the lighter side of Pennsylvania politics. (Photo courtesy of Steve McCaw)*



*Director of NIEHS and the National Toxicology Program, Linda Birnbaum, Ph.D., attended the meeting and engaged Penning with questions about fracking and ground water contamination. (Photo courtesy of Steve McCaw)*



*NCSOT vice president, MaryJane Selgrade, Ph.D., introduced the coal fly ash presentation. Buchwalter is funded by the Tennessee Valley Authority. (Photo courtesy of Steve McCaw)*



*Jaspers focused her talk on the potential health concerns of e-cigarettes and the flavors people inhale along with nicotine. In addition to her NIEHS respiratory research, Jaspers is supported by a National Institutes of Health and a FDA Tobacco Centers of Regulatory Science grant. (Photo courtesy of Steve McCaw)*

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# Summit attendees translate big data into useful knowledge

By Catherine Sprankle

Some 30 NIEHS scientists joined more than 200 representatives from industry, academia, regulatory agencies, and nongovernmental organizations Sept. 29-30 for a workshop at the U.S. Environmental Protection Agency (EPA) in Research Triangle Park, North Carolina.

The [workshop](#) was the agency's Second Data Summit. The summit provided an opportunity for researchers to share ideas about translating massive amounts of new chemical data generated by EPA's Toxicity Forecaster (ToxCast) program into knowledge that can inform policy and regulatory decisions.

[ToxCast](#) uses high-speed, automated screening technologies, or assays, to identify chemicals that trigger biological activity that may lead to adverse health effects. To date, more than 2,000 chemicals have been evaluated in 700 assays. The data from these tests were made publicly available, and the data summit was the first opportunity for researchers to present the results of research projects using this data.

## Presenters discuss research and regulation

NIEHS staff and grantees were key contributors to platform presentations. National Toxicology Program (NTP) Interagency [Center](#) for the Evaluation of Alternative Toxicological Methods director Warren Casey, Ph.D., summarized work by center staff relating ToxCast assay data to the potential health effects of chemicals that interact with the body's estrogen receptor.

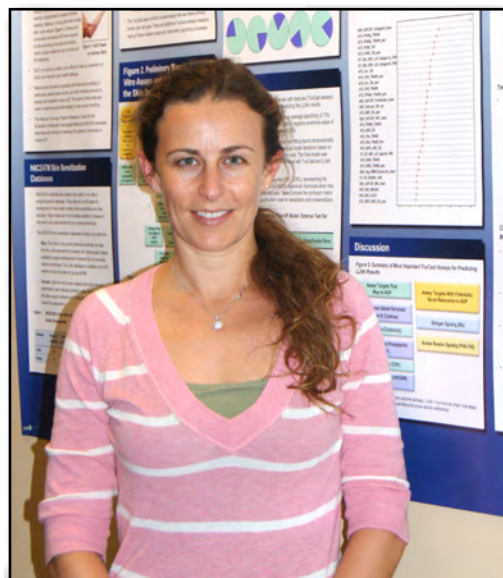
"These assays generate lots of data, but how do we put it all together?" he asked. "We need to identify the assays measuring the interactions that are driving the toxicity responses, [because] the ultimate goal is to run the fewest assays that provide the most information for the least cost."

Robert Tanguay, Ph.D., one of four NIEHS grantees presenting at the meeting, discussed lessons learned from his experiments using zebrafish embryos, in automated tests, to evaluate the biological effects of ToxCast chemicals. He explained the ways in which his laboratory is increasing the content of these assays, by deriving more endpoints from a single exposure. He said that one of the major challenges of the system is determining the internal dose that causes the adverse effect.

While the meeting focused on research presentations, a key theme was the potential for knowledge coming from this research to influence regulation and policy. In his keynote presentation, Jim Jones, assistant administrator for the EPA Office of Chemical Safety and Pollution Protection, provided a regulatory perspective on ToxCast, describing ways information derived from ToxCast data will help fulfill the goals of the agency's Endocrine Disruptor Screening Program.

## Finding alternatives to animal testing

Federal agencies work to reduce the use of animals in research and testing. Methods that use fewer or no animals, or that reduce animal pain and distress, are referred to as [alternative methods](#). The NTP Interagency [Center](#) for the Evaluation of Alternative Toxicological Methods supports the program's high-throughput screening projects and conducts other projects relevant to test method development.



Nicole Kleinstreuer, Ph.D., displays her award-winning poster, "Predicting Skin Sensitization Using ToxCast Assays." Kleinstreuer, a member of the NTP center's ILS contract support team, was also co-author of another award-winning poster presented by EPA scientists. (Photo courtesy of Catherine Sprankle)

## Posters and breakout groups enabled detailed discussions

In addition to two days of speakers, a poster session featured 77 presentations by researchers from throughout the U.S., Canada, and Europe. A total of 18 NIEHS staff and contractors contributed to 13 posters at the meeting, on topics including developmental toxicity, endocrine disruption, and testing prioritization. A poster by NTP scientists, discussing how they used ToxCast data to identify chemicals with the potential to cause allergic contact dermatitis, was one of six posters recognized with an Exemplary Poster Award.

The meeting also provided researchers with specific and practical information. Robert Kavlock, Ph.D., deputy assistant administrator for science in the EPA Office of Research and Development, presented a new ToxCast analysis workflow. Technical breakout groups presented details about the program's assays and chemicals, and instructions for downloading data.

Organizers will soon add slides and video from the meeting to materials already available on the workshop [website](#). A report from the workshop will also be developed.

(Catherine Sprankle is a communications specialist with ILS Inc., support contractor for the NTP center.)

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## Nanotechnology work leads to award for NIEHS grantee


By Joe Balintfy

Somenath Mitra, Ph.D., NIEHS-funded researcher and distinguished professor at the New Jersey Institute of Technology (NJIT), received an Excellence in Research Prize and Medal Oct. 2 from the NJIT Board of Overseers.

Mitra's current research with Andrij Holian, Ph.D., director of the University of Montana [Center](#) for Environmental Health Sciences, is aimed at understanding potential health implications of carbon nanotubes used in diverse applications.





*"You have to balance economics, technology, and the environment and that is my goal ... a sustainable earth and, at the same time, excellent technology so we can live better," said Mitra, center, with Philip Rinaldi, chair of the NJIT Board of Overseers, left, and NJIT President Joel Bloom, Ph.D., right. (Photo courtesy of Deric Raymond, NJIT)*



**Linked video:**  
[Watch Mitra discuss his research on new applications and safe technology for carbon nanotubes in this NJIT video. \(5:52\)](#)

(Launches in new window)

Download Media Player:  Flash 

"His work is important for the public and research community, so we can have a better understanding of the possible impact and safety of carbon nanotubes," said Srikanth Nadadur, Ph.D., health scientist administrator and program lead for nanotechnology in the NIEHS Division of Extramural Research and Training. "Carbon nanotubes are increasingly common in medicine, industry, and consumer products, because of their unique chemical and physical properties." Those same properties may pose unique and unknown health risks.

## Recognizing a broad scope of achievement

[Mitra](#) has achieved wide recognition for his work in air and water monitoring, and diverse application of nanotubes, ranging from solar cell technology to seawater desalination. His work in real-time trace measurement, including development of a variety of sensors for measuring ambient air and industrial emissions at the parts-per-billion level, plays a central role in environmental monitoring.

Recent work in the area of microwave-induced carbon nanotube purification and functionalization has wide-ranging applications in areas from polymer composites to thin films and nanoelectronics. A related development was using carbon nanotube composites to develop solar cells that can be painted on flexible materials.

“His pioneering work has spanned a very impressive spectrum of applications for carbon nanotechnology, which address critical quality-of-life issues, including energy, water purification, and environmental monitoring,” said Donald Sebastian, Ph.D., senior vice president for technology and economic development at NJIT, and president and CEO of the New Jersey Innovation Institute. “He has been instrumental in developing technology for photovoltaic cells — solar cells — so thin and flexible that they might be output on a printer at home to provide household power, when exposed to the sun.”

(This story includes content from an NJIT [news release](#), used by permission. Joe Balintfy is a public affairs specialist in the NIEHS Office of Communications and Public Liaison.)

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## This month in EHP

The November issue of Environmental Health Perspectives ([EHP](#)) addresses environmental aspects of stunted growth and the major source of water pollution — nitrogen and phosphorous.

### Beyond Malnutrition: The Role of Sanitation in Stunted Growth

Stunted growth affects an estimated 165 million children worldwide. Reducing stunting is a global priority for international health organizations and donors, but it is clear that nutritional interventions alone will not get the job done. That is because stunting is not just a nutritional problem, but also an environmental one.

### Nutrient Pollution: A Persistent Threat to Waterways

Forty-two years after the passage of the Clean Water Act, we have yet to make a dent in the major source of pollution of our rivers, lakes, and coastal sounds — the nutrients nitrogen and phosphorus. An array of best management practices is being used to reduce nutrient pollution into waterways, but more is needed.



*Nadadur leads the NIEHS Nano Environmental Health and Safety program, which supports research on nanomaterials. (Photo courtesy of Steve McCaw)*





## Featured research and related news articles this month include:

- PCBs and Impaired Cochlear Function in Children: Comparing Pre- and Postnatal Exposures
- Thinking One Step Ahead: Strategies to Strengthen Epidemiological Data for Use in Risk Assessment
- More Fat, Less Bone? Obesogens May Deliver a One-Two Punch
- Focusing on the AhR [Aryl Hydrocarbon Receptor]: A Potential Mechanism for Immune Effects of Prenatal Exposures



<http://twitter.com/ehponline>

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## Upcoming Falk Lecture to feature Frank Gonzalez

*By Kelly Lenox*

The 2014 Hans L. Falk Memorial Lecture Nov. 18 at NIEHS will feature Frank Gonzalez, Ph.D., head of the National Cancer Institute (NCI) Center for Cancer Research Laboratory of Metabolism. Hosted by Masahiko Negishi, Ph.D., head of the NIEHS Pharmacogenetics Group, Gonzalez will share insights from his research on cytochrome P450 and xenobiotic receptors in drug metabolism and chemical carcinogenesis.

After completing his Ph.D. at the university of Wisconsin in Madison, [Gonzalez](#) worked as a staff fellow at the National Institute of Child Health and Human Development, prior to joining NCI. Gonzalez holds a number of awards and honorary degrees, including the Rawls Palmer Progress in Medicine Award from the American Society for Clinical Pharmacology, and the John J. Abel Award and the Bernard B. Brodie Award in Drug Metabolism from the American Society of Pharmacology and Experimental Therapeutics.

He is the co-inventor on 16 patents and, according to Negishi, has published 792 peer-reviewed studies in journals such as Nature, Science, and Cell Metabolism.

### Metabolism, metabolomics, and cancer

Gonzalez and his team at NCI study drug and carcinogen metabolism and mechanisms of chemical carcinogenesis, primarily using mouse models. They also study metabolic diseases such as obesity, insulin resistance, and fatty liver disease, all of which are risk factors for cancer and increase mortality in cancer patients. Recent studies have uncovered a novel nuclear receptor-driven pathway by which the gut microbiota influence these metabolic diseases, which has led to new insights into potential clinical interventions for these disorders.



*Studies by Gonzalez and his team have revealed that cytochromes P450 mediate the toxicity and carcinogenicity of chemicals and thus have a role in cancer susceptibility. Cytochromes P450 are involved in metabolism of most therapeutically-used drugs, toxicants, and carcinogens. (Photo courtesy of NCI)*

“Frank is a true leader who has opened new directions for the research of xenobiotic metabolism and toxicity, from biochemical characterization of enzymes, to molecular cloning of complementary DNA and genes, to utilizing mouse models and metabolomics,” said Negishi.

The lecture series is named for Hans Falk, Ph.D., who joined NIEHS in 1967 and made important contributions to the emerging field of environmental health science during his tenure as the Institute’s first scientific director. Initiated by scientists and friends of Falk, the annual memorial lecture series features noted guest speakers who have made significant contributions to environmental health science research, among them several Nobel Prize winners.

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## Extramural papers of the month

*By Nancy Lamontagne*

- [BPA linked with endometriosis](#)
- [Uranium exposure linked with lupus](#)
- [Predicting placement of epigenetic modifications](#)
- [Environment stronger than genetics for eosinophilic](#)

Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

### BPA linked with endometriosis

An NIEHS grantee and colleagues reported that higher urinary BPA levels are associated with increased risk of nonovarian pelvic endometriosis. Endometriosis is an estrogen-driven and often painful condition in which tissue that normally lines the uterus grows in other locations in the body.

Previous studies of BPA and endometriosis have shown inconsistent results and had various limitations, including small sample size. For the new study, the researchers used data from the Women’s Risk of Endometriosis study, which is a population-based, case-control study of endometriosis, conducted among females enrolled in a large health care system. They compared urinary BPA levels in 143 women with surgically confirmed endometriosis, and 287 randomly selected study participants without endometriosis.

The investigators observed statistically significant positive associations between urinary BPA concentrations and nonovarian pelvic endometriosis (second versus lowest quartile: OR 3.0; 95% CI: 1.2, 7.3; third versus lowest quartile: OR 3.0; 95% CI: 1.1, 7.6). There was no statistically significant association between total urinary BPA concentration and endometriosis, overall, or ovarian endometriosis. The researchers say that the association between urinary BPA concentration and nonovarian pelvic endometriosis suggests that BPA may affect normal structural changes of hormonally responsive endometrial tissue during the menstrual cycle, promoting establishment and persistence of refluxed endometrial tissue in people with nonovarian pelvic endometriosis.

*Citation:* [Upson K, Sathyanarayana S, De Roos AJ, Koch HM, Scholes D, Holt VL](#). 2014. A population-based case-control study of urinary bisphenol A concentrations and risk of endometriosis. *Hum Reprod* 29(11):2457-2464.

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# Uranium exposure linked with lupus

Researchers, funded in part by NIEHS, report a link between uranium exposure and systemic lupus erythematosus in people living near a former uranium processing facility. The study offers insight into the types of environmental exposures that may contribute to lupus.

The researchers studied the Fernald Community Cohort, which consists of people who lived near a uranium ore processing plant in Fernald, Ohio, while it was operating. The Fernald Community Cohort was monitored for 18 years, providing an ideal group for studying environmental exposures to uranium. The study included 4,187 people with background uranium exposure, 1,273 with moderate exposure, and 2,756 with higher exposure. Anyone who worked at the plant was excluded.

The investigators found a nearly four-fold increase in odds of lupus in people with the highest levels of uranium exposure (OR 3.92, 95% CI 1.131-13.588,  $p = 0.031$ ) compared to people with minimal exposure. Twelve of the 25 systemic lupus erythematosus cases identified came from the higher exposure group. The researchers say that the relationship between high uranium exposure and lupus may come from possible autoimmune, estrogenic, or epigenetic effects of uranium, acquired mutations, or an unidentified accompanying exposure.

*Citation:* [Lu-Fritts PY](#), [Kottyan LC](#), [James JA](#), [Xie C](#), [Buckholz JM](#), [Pinney SM](#), [Harley JB](#). 2014. Systemic lupus erythematosus is associated with uranium exposure in a community living near a uranium processing plant: a nested case-control study. *Arthritis Rheumatol*; doi:10.1002/art.38786 [Online 7 August 2014].

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# Predicting placement of epigenetic modifications

An NIEHS grantee and colleagues have developed a way to predict which DNA sequences are likely to contain epigenetic modifications. Scientists could use this information to edit these sequences, which would reveal more about how these sections of DNA regulate epigenetic modifications that control gene expression.

Epigenetic modifications change how genes are expressed, without changing the DNA code. These alterations include histone modifications and DNA methylation, and they play critical roles in development, disease, and other biological processes. By comparing DNA sequences with and without epigenetic modifications, the researchers identified specific sequences that are recognized by the DNA-binding proteins that specify exactly where other enzymes make epigenetic modifications. The researchers call their new analysis approach Epigram, and have made it and the DNA sequences they identified openly available to other scientists [online](#).

The scientists said their study provides the first catalog of DNA sequences that could be used to guide epigenome editing, which might one day link variations in DNA sequence with epigenomic effects that lead to disease.

*Citation:* [Whitaker JW](#), [Chen Z](#), [Wang W](#). 2014. Predicting the human epigenome from DNA motifs. *Nat Methods*; doi:10.1038/nmeth.3065 [Online 21 September 2014].

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# Environment stronger than genetics for eosinophilic

Researchers have found that the environment plays more of a role than genetics in eosinophilic esophagitis, a severe, chronic allergic inflammatory disease that renders people unable to eat a wide variety of foods. A better understanding of the risk factors for this disease could lead to better strategies for prevention and management, and possibly identify modifiable environmental risk factors.

Although evidence suggests that eosinophilic esophagitis involves both genetic and environmental factors, scientists did not know the extent of the relative contribution. To study gene and environment contributions, the researchers used a cohort of families at the Cincinnati Center for Eosinophilic Disorders at Cincinnati Children's Hospital Medical Center. They also established a new separate cohort with histologically confirmed eosinophilic esophagitis in at least one twin or triplet.

The researchers found that 2.4 percent of siblings and 1.8 percent of first-degree relatives of patients with eosinophilic esophagitis also had the disease. Brothers, fathers, and males were more likely to have the disease than sisters, mothers, or females. Twins had 20 to 40 percent increased risk of the disease, depending upon whether they were identical or fraternal. Both the family and twin analyses supported a genetic contribution to eosinophilic esophagitis risk. Analysis of the twin cohort revealed genetic heritability contributed 14.5 percent of the variability, while environmental factors were responsible for 81 percent. These findings show that much of the familial clustering seen with this disease is due to a shared environment.

*Citation:* Alexander ES, Martin LJ, Collins MH, Kottyan LC, Sucharew H, He H, Mukkada VA, Succop PA, Abonia JP, Foote H, Eby MD, Grotjan TM, Greenler AJ, Dellon ES, Demain JG, Furuta GT, Gurian LE, Harley JB, Hopp RJ, Kagalwalla A, Kaul A, Nadeau KC, Noel RJ, Putnam PE, von Tiehl KF, Rothenberg ME. 2014. Twin and family studies reveal strong environmental and weaker genetic cues explaining heritability of eosinophilic esophagitis. *J Allergy Clin Immunol*; doi:10.1016/j.jaci.2014.07.021 [Online 22 September 2014].

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

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## Intramural papers of the month

*By Tara Ann Cartwright, Monica Frazier, Simone Otto, Qing Xu, and Annah Wyss*

- [NTP helps develop technique for detecting chemicals that disrupt testis function](#)
- [Pesticide use may increase depression risk among farmers](#)
- [DNA replication errors in yeast offer new insight into cancer research](#)
- [Genistein exposure alters the action of glucocorticoids](#)
- [Orphan receptor regulates lipid metabolism](#)

## NTP helps develop technique for detecting chemicals that disrupt testis function

Scientists from the National Toxicology Program and the U. S. Environmental Protection Agency have developed and validated a screening process to identify potential disruptors of fetal testosterone synthesis and testis gene expression *in utero*. Called the Fetal Phthalate Screen, the protocol identifies causes of phthalate syndrome, a condition in which exposure to phthalate esters (PEs) decreases testosterone production during genital development, resulting in abnormalities after birth.

PEs are found in a variety of products used every day, including medical supplies, toys, and personal care products. The goal of this study was to help the EPA in their evaluation of PEs in products and the potential need for policy to control their use.

During the course of 2-3 years, 27 chemicals were assessed by measuring maternal rodent weight gain, fetal viability, and testis testosterone production levels *ex vivo* after PE exposure. The screen accurately quantitated the effects of PEs with known consequence, and also evaluated a series of chemicals for the first time.

Other methodologies exist for identifying chemicals that result in phthalate syndrome, but this screen does it more accurately with greater efficiency, and uses fewer animals than previous techniques. (MF)

*Citation:* Furr JR, Lambright CS, Wilson VS, Foster PM, Gray LE Jr. 2014. A short-term in vivo screen using fetal testosterone production, a key event in the phthalate adverse outcome pathway, to predict disruption of sexual differentiation. *Toxicol Sci* 140(2):403-424.

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## Pesticide use may increase depression risk among farmers

In a recent study, NIEHS scientists reported that farmers exposed to certain types of pesticides may have an increased risk for depression. Pesticides are hypothesized to affect neurotransmission, and several previous epidemiologic studies have found positive associations between use of pesticides and depression.

Using data from the Agricultural Health Study, the investigators examined use of 10 pesticide classes comprising 50 specific pesticides among a large cohort of 21,208 male licensed pesticide applicators, mainly farmers, from North Carolina and Iowa. Among this cohort, 19,506 never reported being diagnosed with depression by a physician, while 1,702 reported a physician diagnosis of depression at baseline or during follow-up.

Ever use of 2 classes of pesticides, fumigants and organochlorine insecticides, and 7 specific pesticides — the fumigants aluminum phosphide and ethylene dibromide; the phenoxy herbicide 2,4,5-T; and the insecticides dieldrin, diazinon, malathion, and parathion — were associated with elevated risk of depression. Risk of depression also appeared to increase with the number of cumulative days of any pesticide use, and was heightened for those ever diagnosed with pesticide poisoning or reporting an incident of unusually high personal pesticide exposure.

This large and comprehensive study supports previous research by indicating an elevated risk of depression among farmers who use pesticides, while highlighting classes and specific pesticides that may warrant follow-up in animal studies. (AW)

*Citation:* [Beard JD, Umbach DM, Hoppin JA, Richards M, Alavanja MC, Blair A, Sandler DP, Kamel F. 2014. Pesticide exposure and depression among male private pesticide applicators in the Agricultural Health Study. Environ Health Perspect 122\(9\):984-991.](#)

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## DNA replication errors in yeast offer new insight into cancer research

Researchers at NIEHS have discovered new information regarding the rates of errors yeasts can make during DNA replication and the efficiency with which the mismatch repair system (MMR) can correct these errors. The findings could help better understand mutations in both evolution and human cancers and better identify mutations that drive cancer formation.

Starting from multiple genomic origins, DNA polymerases use existing DNA strands as templates during synthesis of new strands via serial addition of complementary nucleotides. Despite very high polymerase accuracy and MMR efficiency, errors slip through and cause mutations. Mutations and epigenetic changes in polymerase and MMR genes can dramatically increase both the risk of cancer and mutation rates in affected tumors.

By sequencing 70 nuclear genomes from 8 yeast strains with a variety of MMR and polymerase defects, researchers in this study collected an unprecedented 40,000 mutations. From observed error rates, they concluded that MMR corrects more than 99 percent of all mismatches. They found that MMR efficiency and replication fidelity are both influenced by mismatch type, the responsible polymerase, timing of replication, and replication origin proximity. Mutation rates also vary by replication fork direction, protein coding state, nucleosome proximity, and sequence context. Mutation patterns established in this work explain patterns in hypermutated endometrial cancers. (QX)

*Citation:* [Lujan SA, Clausen AR, Clark AB, MacAlpine HK, MacAlpine DM, Malc EP, Mieczkowski PA, Burkholder AB, Fargo DC, Gordenin DA, Kunkel TA. 2014. Heterogeneous polymerase fidelity and mismatch repair bias genome variation and composition. Genome Res; doi:10.1101/gr.178335.114 \[Online 12 September 2014\].](#)

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## Genistein exposure alters the action of glucocorticoids

Researchers from NIEHS have identified a novel mechanism by which genistein, an estrogen-like molecule naturally found in soy products, regulates glucocorticoid receptor (GR) mediated gene expression. Genistein competes with estradiol for estrogen receptor (ER) binding and is associated with reduced fertility and uterine pathologies. The findings appeared in *Environmental Health Perspectives*.

The authors used microarray analysis to show that genistein exposure induced a different transcriptional response in Ishikawa cells compared to estradiol. In fact, the genes regulated by genistein belong to distinct networks involved in biological pathways. The scientists observed a unique pattern of gene regulation in response to co-administration of genistein and the synthetic glucocorticoid dexamethasone compared to estradiol and dexamethasone.



They also demonstrated that genistein alters glucocorticoid regulation of GR-target genes and found that both GR and ERalpha, one of two specific estrogen receptors, were required to regulate a select set of genes by genistein and dexamethasone.

Taken together, the findings from this study provide an *in vitro* model for understanding the mechanistic actions of genistein. More importantly, the identification of co-regulated genes by microarray analysis provides novel molecular targets for future studies. **(TAC)**

*Citation:* Whirlledge S, Senbanjo LT, Cidlowski JA. 2014. Genistein disrupts glucocorticoid receptor signaling in human uterine endometrial Ishikawa cells. *Environ Health Perspect*; doi:10.1289/ehp.1408437 [Online 19 August 2014].

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## Orphan receptor regulates lipid metabolism

According to NIEHS scientists and their collaborators, retinoic-acid related orphan receptor-gamma (RORgamma) helps regulate lipid metabolism in the liver and serves as an important link between the circadian clock and the regulation of several lipid metabolic genes.

Previous studies showed that RORgamma exhibits a rhythmic pattern of expression that is controlled by the circadian clock, but its physiological function was poorly understood. Scientists fed RORgamma knockout mice and their control wild-type littermates a high fat diet or a normal diet, and analyzed gene expression and lipid levels in the liver at different intervals throughout the day. This study found that the rhythmic expression of RORgamma corresponded to the rhythmic expression of several genes important in lipid metabolism. This rhythmic regulation was greatly abolished in RORgamma knockout mice and resulted in significant changes in the level of several blood and hepatic lipids.

The investigators further demonstrated that some of these genes were indirectly regulated, while others were directly regulated by RORgamma through retinoic-acid orphan receptor response elements in their promoter regulatory region. The study reveals an important function for RORgamma in the rhythmic regulation of lipid metabolism and suggests a regulatory role for RORgamma in metabolic syndrome. **(SO)**

*Citation:* Takeda Y, Kang HS, Lih FB, Jiang H, Blaner WS, Jetten AM. 2014. Retinoid acid-related orphan receptor gamma, RORgamma, participates in diurnal transcriptional regulation of lipid metabolic genes. *Nucleic Acids Res* 42(16):10448-10459.

(Tara Ann Cartwright, Ph.D., is a former postdoctoral fellow in the NIEHS Intracellular Regulation Group. Monica Frazier, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Mechanisms of Mutation Group. Simone Otto, Ph.D., is an IRTA fellow in the NIEHS Ion Channel Physiology Group. Qing Xu is a biologist in the NIEHS Metabolism, Genes, and Environment Group. Annah Wyss, Ph.D., is an IRTA fellow in the NIEHS Genetics, Environment, and Respiratory Disease Group.)

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# Inside the Institute

## NIEHS celebrates 2014 Fall Fest

*By Ian Thomas*

Scientists and employees from across the institute flocked to NIEHS main building Oct. 23 for the 2014 Fall Fest. The four-hour event featured Combined Federal Campaign (CFC) charities, community service groups, and vendors, as well as canoeing, kayaking, and stand-up paddleboarding on Discovery Lake.

“Events like this allow our employees to really get to know the organizations they’re supporting through CFC, and interact with many others within our local community,” said Claire Long, an employee services specialist with the NIEHS Administrative Services and Analysis Branch.

Long coordinated the event with colleagues Ed Kang, Jenn Evans, Cynthia Radford, and A’tondra Caree.

### A community affair

In addition to raising funds for CFC, Fall Fest also sought to unite NIEHS employees with other charities and local support organizations from around the North Carolina Triangle area. In all, representatives from more than 60 organizations were on hand to pass out literature and answer questions.

“This is our first year of affiliation with Fall Fest and it’s been an amazing experience so far,” said Terry Morris of Vets to Vets United, a CFC organization that unites veterans suffering from post-traumatic stress with animals in need of a loving companion and home. “From new recruiting efforts to networking opportunities with other charities, CFC has allowed us to take our mission of helping America’s vets to a lot of places it might not have otherwise gone.”

(Ian Thomas is a public affairs specialist for the NIEHS Office of Communication and Public Liaison, and a regular contributor to the Environmental Factor.)



*Clyde Hasty of the NIEHS Health and Safety Branch asked questions at an information table set up outside the main building. (Photo courtesy of Steve McCaw)*



*A team from NC First Robotics showed off Spitfire, a robotic basketball player. (Photo courtesy of Steve McCaw)*





*NIEHS employees took part in a number of outdoor activities, courtesy of Frog Hollow Outdoors. (Photo courtesy of Steve McCaw)*



*NIEHS health scientist Rachel Frawley tried out a paddleboard. (Photo courtesy of Steve McCaw)*



*NIEHS fellows Georgia Hinkley, Ph.D., left, and Natasha Catlin, Ph.D., right, made new friends at Fall Fest. (Photo courtesy of Steve McCaw)*



*Chances are this little guy will find a home before long. (Photo courtesy of Steve McCaw)*

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